FIG.1

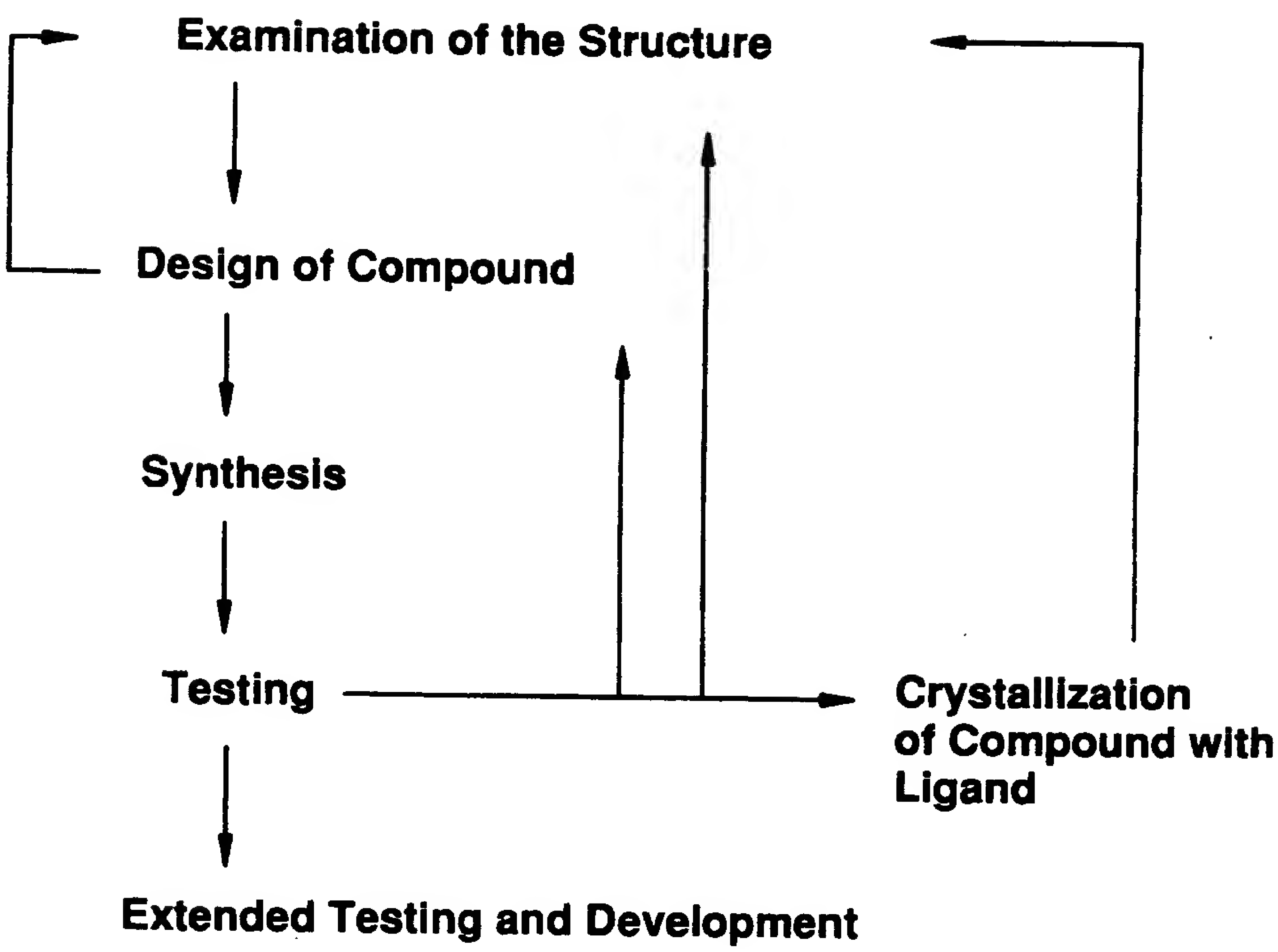

FIG.2

DOMAINS :	NH_2 - TERMINAL	DNA BINDING	LIGAND BINDING
HOMOLOGY :	Hypervariable	> 40%	About 20%
FUNCTION :	Transactivation	DNA Binding Dimerization	LIGAND Binding Dimerization Transactivation Nuclear translocation Hsp binding

```
                1                                                          60
      rTRalpha  .......... .......... .......... .......... .......... ..........
      hTRalpha  .......... .......... .......... .......... .......... ..........
       hTRbeta  .......... .......... .......... .......... .......... ..........
     hRARalpha  .......... .......... .......... .......... .......... ..........
     hRARgamma  .......... .......... .......... .......... .......... ..........
     hRXRalpha  .......... .......... .......... .......... .......... ..........
      hRXRbeta  .......... .......... .......... .......... .......... ..........
    hPPARalpha  .......... .......... .......... .......... .......... ..........
     hPPARbeta  .......... .......... .......... .......... .......... ..........
    hPPARgamma  .......... .......... .......... .......... .......... ..........
          hVDR  .......... .......... .......... .......... .......... ..........
           hER  .......... .......... .......... .......... .......... ..........
           hGR  .......... .......... .......... .......... .......... ..........
           hPR  MTELKAKGPR APHVAGGPPS PEVGSPLLCR PAAGPFPGSQ TSDTLPEVSA IPISLDGLLF
           hMR  ...METKGYH SLPEGLDMER RWGQVSQAVE RSSLGPTERT DENNYMEIVN VSCVSGAIPN
           hAR  .......... .......... .......... .......... .......... ..........
```

FIG.3A

```
                61                                                                  120
      rTRalpha  .......... .......... .......... .......... .......... ..........
      hTRalpha  .......... .......... .......... .......... .......... ..........
       hTRbeta  .......... .......... .......... .......... .......... ..........
     hRARalpha  .......... .......... .......... .......... .......... ..........
     hRARgamma  .......... .......... .......... .......... .......... ..........
     hRXRalpha  .......... .......... .......... .......... .......... ..........
      hRXRbeta  .......... .......... .......... .......... .......... ..........
    hPPARalpha  .......... .......... .......... .......... .......... ..........
     hPPARbeta  .......... .......... .......... .......... .......... ..........
    hPPARgamma  .......... .......... .......... .......... .......... ..........
          hVDR  .......... .......... .......... .......... .......... ..........
           hER  .......... .......... .......... .......... .......... ..........
           hGR  .......... .......... .....MDSKE SLTPGREENP SSVLAQERGD VMDFYKTLRG
           hPR  PRPCQGQDPS DEKTQDQQSL SDVEGAYSRA EATRGAGGSS SSPPEKDSGL LDSVLDTLLA
           hMR  NSTQGSSKEK QELLPCLQQD NNRPGILTSD IKTELESKEL SATVAESMGL YMDSVRDADY
           hAR  .......... .......... .......... .......... .......... ..........
```

FIG.3B

```
                121                                                                 180
      rTRalpha  .......... .......... .......... .......... .......... ..........
      hTRalpha  .......... .......... .......... .......... .......... ..........
       hTRbeta  .......... .......... .......... .......... .......... ..........
     hRARalpha  .......... .......... .......... .......... .......... ..........
     hRARgamma  .......... .......... .......... .......... .......... ..........
     hRXRalpha  .......... .......... .......... .......... .......... ..........
      hRXRbeta  .......... .......... .......... .......... .......... ..........
    hPPARalpha  .......... .......... .......... .......... .......... ..........
     hPPARbeta  .......... .......... .......... .......... .......... ..........
    hPPARgamma  .......... .......... .......... .......... .......... ..........
          hVDR  .......... .......... .......... .......... .......... ..........
          hER   .......... .......... .......... .......... .......... ..........
          hGR   GATVKVSASS PSLAVASQS. .......... .......... .DSKQRRLLV DFPKGSVSNA
          hPR   PSGPGQSQPS PPACEVTSSW CLFGPELPED PPAAPATQRV LSPLMSRSGC KVGDSSGTAA
          hMR   SYEQQNQQGS MSPAKIYQNV EQLVKFYKGN GHRPSTLSCV NTPL..RSFM SDSGSSVNGG
          hAR   .......... .......... .......... .......... .......... ..........
```

FIG.3C

```
                181                                                       240
      rTRalpha  .......... .......... .......... .......... .......... ..........
      hTRalpha  .......... .......... .......... .......... .......... ..........
       hTRbeta  .......... .......... .......... .......... .......... ..........
    hRARalpha   .......... .......... .......... .......... .......... ..........
    hRARgamma   .......... .......... .......... .......... .......... ..........
     hRXRalpha  .......... .......... .......... .......... .......... ..........
      hRXRbeta  .......... .......... .......... .......... .......... ..........
   hPPARalpha   .......... .......... .......... .......... .......... ..........
    hPPARbeta   .......... .......... .......... .......... .......... ..........
   hPPARgamma   .......... .......... .......... .......... .......... ..........
         hVDR   .......... .......... .......... .......... .......... ..........
          hER   .......... .......... .......... .......... .......... ..........
          hGR   QQPDLSKAVS LSMGLYMGET ETKVMGNDLG FPQQGQISLS SGETDLKLLE ESIANLNRS.
          hPR   AHKVLPRGLS PARQLLLPAS ESPHWSGAPV KPSPQAAAVE VEEEDSSESE ESAGPLLKGK
          hMR   VMRAIVK..S PIMCHEKSPS VCSPLNMTSS VCSPAGINSV SSTTASFGSF PVHSPITQGT
          hAR   .......... .......... .......... .......... .......... ..........
```

FIG.3D

	241					300
rTRalpha	.....	.....	.....	.....	.....	.....
hTRalpha	.....	.....	.....	.....	.....	.....
hTRbeta	.....	.....	.....	.....	.....	.....
hRARalpha	.....	.....	.....	.....	.....	.....
hRARgamma	.....	.....	.....	.....	.....	.....
hRXRalpha	.....	.....	.....	.....	.....	.....
hRXRbeta	.....	.....	.....	.....	.....	.....
hPPARalpha	.....	.....	.....	.....	.....	.....
hPPARbeta	.....	.....	.....	.....	.....	.....
hPPARgamma	.....	.....	.....	.....	.....	.....
hVDR	.....	.....	.....	.....	.....	.....
hER	.....	.....	.....	.....	.....	.....
hGR	....TSVPEN	PKSSASTAVS	AAPTEKEFPK	THSDVSSEQQ	HLKGQTGTNG	GNVKLYTT..
hPR	PRALGGAAAG	GGAAACPPGA	AAGGVALVPK	EDSRFSAPRV	ALVEQDAPMA	PGRSPLATTV
hMR	PLTCSPNAEN	RGSRSHSPAH	ASNVGSPLSS	PLSSMKSSIS	SPPSHCSVKS	PVSSPNNVTL
hAR	.....	.....	.....	.....	.....	.....

FIG.3E

APPROVED	O.G. FIG.	
BY	CLASS	SUBCLASS
DRAFTSMAN		

```
            301                                                          360
rTRalpha    .......... .......... .......... .......... .......... ..........
hTRalpha    .......... .......... .......... .......... .......... ..........
hTRbeta     .......... .......... .......... .......... .......... ..........
hRARalpha   .......... .......... .......... .......... .......... ..........
hRARgamma   .......... .......... .......... .......... .......... ..........
hRXRalpha   .......... .......... .......... .......... .......... ..........
hRXRbeta    .......... .......... .......... .......... .......... ..........
hPPARalpha  .......... .......... .......... .......... .......... ..........
hPPARbeta   .......... .......... .......... .......... .......... ..........
hPPARgamma  .......... .......... .......... .......... .......... ..........
hVDR        .......... .......... .......... .......... .......... ..........
hER         .......... .......... .......... .......... .......... ..........
hGR         .......... ......DQST FDILQDLEFS SGSPGK.... ........ET NESPWRSDLL
hPR         MDFIHVPILP LNHALLAART RQLLEDESYD GGAGAA.... ........SA FAPPRTSPCA
hMR         RSSVSSPANI NNSRCSVSSP SNTNNRSTLS SPAASTVGSI CSPVNNAFSY TASGTSAGSS
hAR         .......... .......... .......... .......... .......... ..........
```

FIG.3F

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	361					420
rTRalpha	.....	.....	.....	.....	.....	.....
hTRalpha	.....	.....	.....	.....	.....	.....
hTRbeta	.....	.....	.....	.....	.....	.....
hRARalpha	.....	.....	.....	.....	.....	.....
hRARgamma	.....	.....	.....	.....	.....	.....
hRXRalpha	.....	.....	.....	.....	.....	.....
hRXRbeta	.....	.....	.....	.....MSW	AARPPFLPQR	HAEGSVGRWG
hPPARalpha	.....	.....	.....	.....	.....	.....
hPPARbeta	.....	.....	.....	.....	.....	.....
hPPARgamma	.....	.....	.....	.....	.....	.....
hVDR	.....	.....	.....	.....	.....	.....
hER	.....	.....	.....	.....	.....	.....MTM
hGR	IDENCLLSPL	AGEDDSFLLE	GNSNEDCKPL	ILPDTKPKIK	DNGDLVLSSP	SNVTLPQVKT
hPR	SSTPVAVGDF	P..DCAYPPD	AEPKDDAYPL	YSDFQPPALK	IKEEEEGAEA	SARSPRSYLV
hMR	TLRDVVPSPD	TQEKGAQEVP	FPKTEEVESA	ISNGVTGQLN	IVQYIKPEPD	GAFSSSCLGG
hAR	.....	.....	.....	.....	.....	.....

FIG.3G

```
                421                                                                 480
      rTRalpha  .......... .......... .......... .......... .......... ..........
      hTRalpha  .......... .......... .......... .......... .......... ..........
       hTRbeta  .......... .......... .......... .......... .......... ..........
     hRARalpha  .......... .......... .......... .......... .......... ..........
     hRARgamma  .......... .......... .......... .......... .......... ..........
     hRXRalpha  .......... .......... .......... .......... MDTKHFLPLD FSTQVNSS..
      hRXRbeta  AKECIVGSAT ALAGSRSGGG GGGGRRRTTN PGAGARGWTG RDGRH..GRD SRSPDSSSPN
    hPPARalpha  .......... .......... .......... .......... .......... ..........
     hPPARbeta  .......... .......... .......... .......... .......... ..........
    hPPARgamma  .......... .......... .......... .......... .......... ..........
         hVDR   .........M DTEDLPANNA PLTVNEQLLG SCTLKFPAQD AQVIVMSGQE TIRVLEVEVD
          hER   TLHTKASGMA LLHQIQGNEL EPLNRPQLKI PLERPLGEVY LDSSKPAVYN YPEGAAYEFN
          hGR   EKEDFIELCT PGVIKQEKLG TVYCQASFPG ANIIG..... .........NK MSAISVHGVS
          hPR   AGANPAAFPD FPLGPPPPLP PR.ATPSRPG EAAVT..... .........AA PASASVSSAS
          hMR   NSKINSDSSF SVPIKQESTK HSCSGTSFKG NPTVNPFPFM DGSYFSFMDD KDYASLSGIL
          hAR   .......... .......... ........GG GGGEA..... .........GA VAPYGYTRP.
```

FIG.3H

```
            481                                                         540
  rTRalpha  .......... .......... .......... .......... ...MEQKPSK VECGSDPEEN
  hTRalpha  .......... .......... .......... .......... ...MEQKPSK VECGSDPEEN
   hTRbeta  .......... .......... ..MTPNSMTE NGLTAWDKPK HCPDREHDWK LVGMSEACLH
 hRARalpha  .......... .......... .......... .......... .......... ..........
 hRARgamma  .......... .......... .......... .........M ATNKERLFAA GALGPGSGYP
 hRXRalpha  .LTSPTGR.. GSMAAPSLHP SLGPGIGSPG .QLHSPISTL SSPINGMGPP FSVISSPMGP
  hRXRbeta  PLPQGVPP.. PSPPGPPLPP STAPTLGGSG .APPPP.... PMPPPPLGSP FPVISSSMGS
hPPARalpha  ..MVDTESPL CPLSPLEAGD LESPLSEEFL QEMGNIQEIS QSIGEDSSGS FGFTEYQYLG
 hPPARbeta  .......... .....MEQPQ EEAP...... .EVREEEEKE EVAEAEGAPE LNGGPQHALP
hPPARgamma  .......... .......MVD TEMPFWPTNF ....GISSVD LSMMDDHSHS FDIKPFTTVD
      hVDR  TALSSAGAAE SGGDEEGSGQ SLEATEEAQL DGPVTTSSTT AVTVEVSAPV VQTVVSKAAI
       hER  AAAAANAQVY GQTGLPYGPG SEAAAFGSNG LGGFPPLNSV SPSPLMLLHP PPQLSPFLQP
       hGR  TSGGQMYHYD MNTASLSQQQ DQ........ .KPIFNVIPP IPVGSEN... ..........
       hPR  SSGSTLECIL YKAEGAPPQQ GPFAPPPCKA PGASGCLLPR DGLPSTS... ..........
       hMR  GPPVPGFDGN CEGSGFPVGI KQEPDDGSYY PEASIPSSAI VGVNSGGQSF HYRIGAQGTI
       hAR  .......... ..PQGLAGQE SDFTAPDVWY PGG...MVSR VPYPSPT... ..........
```

FIG.3I

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```
            541                                                        600
  rTRalpha  SARSPDGKRK RKN.GQCP.. .....LKSSM .......... .......... ......SGYI
  hTRalpha  SARSPDGKRK RKN.GQCS.. .....LKTSM .......... .......... ......SGYI
   hTRbeta  RKSHSERRST LKN.EQSSPH LIQTTWTSSI FHLDHDDVND QSVSSAQTFQ TEEKKCKGYI
 hRARalpha  .......... .......... ........PN SNHVASGAGE AAIETQSSSS EEIVPSPPSP
 hRARgamma  GAGFPFAFPG ALR.GSPPFE MLSPSFRGLG QPDLPKEMAS LSVETQSTSS EEMVPSSPSP
 hRXRalpha  HSMSVP.... .TTPTLGFST GSPQLSS... .PMNPVSSSE DIKPPLGLNG VLKVPAHPSG
  hRXRbeta  PGLPPP.... .APPGFSGPV SSPQINSTVS LPGGGSGPPE DVKPPVLGVR GLHCPPPPGG
hPPARalpha  SCPGSDGSVI TDTLSPA... .......... .......... .SSPS..SVT YPVVPGSVDE
hPPARbeta   SSSYTD.... ...LSRS... .......... .......... .SSPP..SLL DQLQMGC.DG
hPPARgamma  FSSISAPHYE DIPFTRADPM VADYKYDLKL QEYQSAIKVE PASPPYYSEK AQLYNRPHEE
      hVDR  SVSPAQQTSV PITVQACPQV LTQDGLASLM TGMLAQQSSL GQPLLIPLSM AGSVGGQGGL
       hER  HGQQVPYYLE NEPSGYTVRE AGPP....AF YRPNSDNRRQ GGRERLASTN DKGSMAMESA
       hGR  ..WNRCQGSG DDNLTSLGTL NFPGRTVFSN GYSSPSMRPD V.......... .SSPPSSSST
       hPR  ..ASAAAAGA APALYPALGL NGLPQLGYQA AVLKEGLPQV YPPYLNYLRP DSEASQSPQY
       hMR  SLSRSARDQS FQHLSSFPPV NTLVESWKSH GDLSSRRSDG YPVLEYIPEN VSSSTLRSVS
       hAR  ..CVKSEMGP WMDSYSG... ......PYGD MRLETARDHV LP..IDYYFP ..........
```

FIG.3J

```
           601                                                                660
rTRalpha   PSYLDKDEQC VVCGDKATGY HYRCITCEGC KGFFRRTIQK NLHPTYSCKY DS........
hTRalpha   PSYLDKDEQC VVCGDKATGY HYRCITCEGC KGFFRRTIQK NLHPTYSCKY DS........
hTRbeta    PSYLDKDELC VVCGDKATGY HYRCITCEGC KGFFRRTIQK NLHPSYSCKY EG........
hRARalpha  PPLPRIYKPC FVCQDKSSGY HYGVSACEGC KGFFRRSIQK NM..VYTCHR DK........
hRARgamma  PPPPRVYKPC FVCNDKSSGY HYGVSSCEGC KGFFRRSIQK NM..VYTCHR DK........
hRXRalpha  NMASFTKHIC AICGDRSSGK HYGVYSCEGC KGFFKRTVRK DL..TYTCRD NK........
hRXRbeta   PGAG..KRLC AICGDRSSGK HYGVYSCEGC KGFFKRTIRK DL..TYSCRD NK........
hPPARalpha SPSGALNIEC RICGDKASGY HYGVHACEGC KGFFRRTIRL KLVYD...KC DR........
hPPARbeta  ASCGSLNMEC RVCGDKASGF HYGVHACEGC KGFFRRTIRM KLEYE...KC ER........
hPPARgamma PSNSLMAIEC RVCGDKASGF HYGVHACEGC KGFFRRTIRL KLIYD...RC DL........
hVDR       AVLTLPTATV ATLPGLAAAS PAGGLLKLPF AGLQAATVLN SVQTQLQAPA QAVLQPQMSA
hER        KET....RYC AVCNDYASGY HYGVWSCEGC KAFFKRSIQG HN..DYMCPA TN........
hGR        ATTGPPPKLC LVCSDEASGC HYGVLTCGSC KVFFKRAVEG QHNYLCAGRN D.........
hPR        SFESLPQKIC LICGDEASGC HYGVLTCGSC KVFFKRAMEG QHNYLCAGRN D.........
hMR        TGSSRPSKIC LVCGDEASGC HYGVVTCGSC KVFFKRAVEG QHNYLCAGRN D.........
hAR        .....PQKTC LICGDKASGC HYGALTCGSC KVFFKRAAEG KQKYLCASRN D.........
```

FIG.3K

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BY	CLASS	SUBCLASS
DRAFTSMAN		

	661					720
rTRalpha	.CCVIDKITR	NQCQLCRFKK	CIAVGMAMDL	VLDDSKRVAK	RKLIEQNRER	RRK..EEMIR
hTRalpha	.CCVIDKITR	NQCQLCRFKK	CIAVGMAMDL	VLDDSKRVAK	RKLIEQNRER	RRK..EEMIR
hTRbeta	.KCVIDKVTR	NQCQECRFKK	CIYVGMATDL	VLDDSKRLAK	RKLIEENREK	RRR..EELQK
hRARalpha	.NCIINKVTR	NRCQYCRLQK	CFEVGMSKES	VRND......	.......RNK	KKK..EVPKP
hRARgamma	.NCIINKVTR	NRCQYCRLQK	CFEVGMSKEA	VRND......	.......RNK	KKK..EVKEE
hRXRalpha	.DCLIDKRQR	NRCQYCRYQK	CLAMGMKREA	VQEERQRG..	....KDRNEN	EVE..STSSA
hRXRbeta	.DCTVDKRQR	NRCQYCRYQK	CLATGMKREA	VQEERQRG..	....KDK.DG	DGE..CAGGA
hPPARalpha	.SCKIQKKNR	NKCQYCRFHK	CLSVGMSHNA	IRFG......	.RMPRSEKAK	LKA..EILTC
hPPARbeta	.SCKIQKKNR	NKCQYCRFQK	CLALGMSHNA	IRFG......	.RMPEAEKRK	LVA..GLTAN
hPPARgamma	.NCRIHKKSR	NKCQYCRFQK	CLAVGMSHNA	IRFG......	.RMPQAEKEK	LLA..EI.SS
hVDR	LQAMQQTQTT	AATTASIVQK	ASEPSVSVAT	LQTAGLSINP	AIISAASLGA	QPQFISSLTT
hER	.QCTIDKNRR	KSCQACRLRK	CYEVGMMKGG	IRKDRRGGRM	LKHKRQRDDG	EGR..GEVGS
hGR	..CIIDKIRR	KNCPACRYRK	CLQAGMNLEA	....	RKTKK..KIK	GIQ..QATT.
hPR	..CIVDKIRR	KNCPACRLRK	CCQAGMVLGG	....	RKFKKFNKVR	VVR..ALDAV
hMR	..CIIDKIRR	KNCPACRLQK	CLQAGMNLGA	....	RKSKKLGKLK	GIH..EEQPQ
hAR	..CTIDKFRR	KNCPSCRLRK	CYEAGMTLGA	....	RKLKKLGNLK	LQE..EGEAS

FIG.3L

minimal start site 725

```
             721                                                                 780
rTRalpha     SLQQRPEPTP EEWDLIHVAT EAHRSTNAQG SHWKQRRKFL PDDIGQSPIV ..........
hTRalpha     SLQQRPEPTP EEWDLIHIAT EAHRSTNAQG SHWKQRRKFL PDDIGQSPIV ..........
hTRbeta      SIGHKPEPTD EEWELIKTVT EAHVATNAQG SHWKQKPKFL PEDIGQAPIV ..........
hRARalpha    ECSESYTLTP EVGELIEKVR KAHQETFPAL CQL...GKYT TNNSSEQRV. ..........
hRARgamma    GSPDSYELSP QLEELITKVS KAHQETFPSL CQL...GKYT TNSSADHRV. ..........
hRXRalpha    NEDMPVERIL EAELAVEPKT ETYVE..ANM GLNPS..... ......SP.. ..........
hRXRbeta     PEEMPVDRIL EAELAVEQKS DQGVEGPGGT GGSGS..... ......SP.. ..........
hPPARalpha   EHDIEDSETA DLKSLAKRIY EAYLKNFN.M NKVKARVILS GKASNNPPFV IHDMETLCMA
hPPARbeta    EGSQYNPQVA DLKAFSKHIY NAYLKNFN.M TKKKARSILT GKASHTAPFV IHDIETLWQA
hPPARgamma   DIDQLNPESA DLRALAKHLY DSYIKSFP.L TKAKARAILT GKTTDKSPFV IYDMNSLMMG
hVDR         TPIITSAMSN VAGLTSQLIT NAQGQVIGTL PLLVNPASLA GAAAASA... .......LPA
hER          AGDMRAANLW PSPLMIKRSK KNSLALSLTA DQMVSALLDA EPPILYSE.. ..........
hGR          .......GVSQ ETSENPGNKT IVPATLPQLT PTLVS..... .......... LL........
hPR          ALPQPLGVPN ESQALSQRFT FSPGQDIQLI PPLIN..... .......... LL........
hMR          QQQPPPPPPP PQSPEEGTTY IAPAKEPSVN TALVPQLSTI SRALTPSPVM VL........
hAR          STTSP..... .TEETTQKLT VSHIEGYECQ PIFLN..... .......... VL........
```

FIG.3M

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DRAFTSMAN | BY | CLASS | SUBCLASS

	781				840
rTRalpha	.....	.SMPDGDKVD	LEAFSEFTKI	ITPAITRVVD	FAKKLPMFSE LPCEDQIILL
hTRalpha	.....	.SMPDGDKVD	LEAFSEFTKI	ITPAITRVVD	FAKKLPMFSE LPCEDQIILL
hTRbeta	.....	.NAPEGGKVD	LEAFSHFTKI	ITPAITRVVD	FAKKLPMFCE LPCEDQIILL
hRARalpha	.....	.....SLD	IDLWDKFSEL	STKCIIKTVE	FAKQLPGFTT LTIADQITLL
hRARgamma	.....	.....QLD	LGLWDKFSEL	ATKCIIKIVE	FAKRLPGFTG LSIADQITLL
hRXRalpha	.....	.NDPVTNICQ	A.....	ADKQLFTLVE	WAKRIPHFSE LPLDDQVILL
hRXRbeta	.....	.NDPVTNICQ	A.....	ADKQLFTLVE	WAKRIPHFSS LPLDDQVILL
hPPARalpha	EKTLVAKLVA	NGIQN.KEVE	VRIFHCCQCT	SVETVTELTE	FAKAIPAFAN LDLNDQVTLL
hPPARbeta	EKGLVWKQLV	NGLPPYKEIS	VHVFYRCQCT	TVETVRELTE	FAKSIPSFSS LFLNDQVTLL
hPPARgamma	EDKIKFKHIT	PLQEQSKEVA	IRIFQGCQFR	SVEAVQEITE	YAKNIPGFIN LDLNDQVTLL
hVDR	QGLQVQTVAP	QLLLNSQGQI	IATIGNGPTA	AIPSTASVLP	KATVPLTLTK TTTQGPVGKV
hER	.....	.YDPTRPFSE	ASMMGLLTNL	ADRELVHMIN	WAKRVPGFVD LTLHDQVHLL
hGR	EVIEPEVLYA	GYDSSVPDST	WRIMTTLNML	GGRQVIAAVK	WAKAIPGFRN LHLDDQMTLL
hPR	MSIEPDVIYA	GHDNTKPDTS	SSLLTSLNQL	GERQLLSVVK	WSKSLPGFRN LHIDDQITLI
hMR	ENIEPEIVYA	GYDSSKPDTA	ENLLSTLNRL	AGKQMIQVVK	WAKVLPGFKN LPLEDQITLI
hAR	EAIEPGVVCA	GHDNNQPDSF	AALLSSLNEL	GERQLVHVVK	WAKALPGFRN LHVDDQMAVI

FIG.3N

	841					900
rTRalpha	KGCCMEIMSL	RAAVRY..DP	ESDTLTLSGE	MTVKRKQLK.	..N..GGLGV	VSDAIFELGK
hTRalpha	KGCCMEIMSL	RAAVRY..DP	ESDTLTLSGE	MAVKREQLK.	..N..GGLGV	VSDAIFELGK
hTRbeta	KGCCMEIMSL	RAAVRY..DP	ESETLTLNGE	MAVIRGQLK.	..N..GGLGV	VSDAIFDLGM
hRARalpha	KAACLDILIL	RICTRY..TP	EQDTMTFSDG	LTLNRTQMH.	..N..AGFGP	LTDLVFAFAN
hRARgamma	KAACLDILML	RICTRY..TP	EQDTMTFSDG	LTLNRTQMH.	..N..AGFGP	LTDLVFAFAG
hRXRalpha	RAGWNELLIA	SFSHRS..IA	VKDGILLATG	LHVHRNSAH.	..S.AGVGAI	FDRVLTELVS
hRXRbeta	RAGWNELLIA	SFSHRS..ID	VRDGILLATG	LHVHRNSAH.	..S.AGVGAI	FDRVLTELVS
hPPARalpha	KYGVYEAIFA	MLSSVM..NK	DGMLVAYGNG	F.ITREFLK.	..SLRKPFCD	IMEPKFDFAM
hPPARbeta	KYGVHEAIFA	MLASIV..NK	DGLLVANGSG	F.VTREFLR.	..SLRKPFSD	IIEPKFEFAV
hPPARgamma	KYGVHEIIYT	MLASLM..NK	DGVLISEGQG	F.MTREFLK.	..SLRKPFGD	FMEPKFEFAV
hVDR	APSKVIIAPQ	PSVVKPVTSL	TAAGVIACGE	MPTVGQLVNK	PSAVKDEEAI	NLEEIREFAK
hER	ECAWLEILMI	GLVWRS..ME	HPGKLLFAPN	LLLDRNQGK.	..CVEGMVEI	FDMLLAT.SS
hGR	QYSWMFLMAF	ALGWRSYRQS	SANLLCFAPD	LIINEQRMT.	....LPCMYD	QCKHMLYVSS
hPR	QYSWMSLMVF	GLGWRSYKHV	SGQMLYFAPD	LILNEQRMK.	....ESSFYS	LCLTMWQIPQ
hMR	QYSWMCLSSF	ALSWRSYKHT	NSQFLYFAPD	LVFNEEKMH.	....QSAMYE	LCQGMHQISL
hAR	QYSWMGLMVF	AMGWRSFTNV	NSRMLYFAPD	LVFNEYRMH.	....KSRMYS	QCVRMRHLSQ

FIG.30

09637132 .081000

BY		
DRAFTSMAN	CLASS	SUBCLASS

	901				960
rTRalpha	SLSAFNLDDT	EVALLQAVLL	MSTD.....	..RSGLLCVD KIEKSQEAYL	LA...FEHYV
hTRalpha	SLSAFNLDDT	EVALLQAVLL	MSTD.....	..RSGLLCVD KIEKSQEAYL	LA...FEHYV
hTRbeta	SLSSFNLDDT	EVALLQAVLL	MSSD.....	..RPGLACVE RIEKYQDSFL	LA...FEHYI
hRARalpha	QLLPLEMDDA	ETGILSAICL	ICGD.....	..RQDLEQPD RVDMLQEPLL	EA...LKVYV
hRARgamma	QLLPLEMDDT	ETGLLSAICL	ICGD.....	..RMDLEEPE KVDKLQEPLL	EA...LRLYA
hRXRalpha	KMRDMQMDKT	ELGCLRAIVL	FNPDS.....	...KGLSNPA EVEALREKVY	AS...LEAYC
hRXRbeta	KMRDMRMDKT	ELGCLRAIIL	FNPDA.....	...KGLSNPS EVEVLREKVY	AS...LETYC
hPPARalpha	KFNALELDDS	DISLFVAAII	CCGD.....	..RPGLLNVG HIEKMQEGIV	HV...LRLHL
hPPARbeta	KFNALELDDS	DLALFIAAII	LCGD.....	..RPGLMNVP RVEAIQDTIL	RA...LEFHL
hPPARgamma	KFNALELDDS	DLAIFIAVII	LSGD.....	..RPGLLNVK PIEDIQDNLL	QA...LELQL
hVDR	NFKIRRLSLG	LTQTQVGQAL	TATEGPAYSQ	SAICRFEKLD ITPKSAQKLK	PVLERWLAEA
hER	RFRMMNLQGE	EFVCLKSIIL	LNSGVYTFLS	STLKSLEEKD HIHRVLDKIT	DTLIHLMAKA
hGR	ELHRLQVSYE	EYLCMKTLLL	LSS.....	VPKDGLKSQE LFDEIRMTYI	KELGKAIVKR
hPR	EFVKLQVSQE	EFLCMKVLLL	LNT.....	IPLEGLRSQT QFEEMRSSYI	RELIKAIGLR
hMR	QFVRLQLTFE	EYTIMKVLLL	LST.....	IPKDGLKSQA AFEEMRTNYI	KELRKMVTKC
hAR	EFGWLQITPQ	EFLCMKALLL	FSI.....	IPVDGLKNQK FFDELRMNYI	KELDRIIACK

FIG.3P

	961					1020
rTRalpha	NHRKHNIPHF	WPKLL....M	KVTDLRMIGA	CHASRFL..H	MKVEC..PTE	LFPPLFLEVF
hTRalpha	NHRKHNIPHF	WPKLL....M	KVTDLRMIGA	CHASRFL..H	MKVEC..PTE	LFPPLFLEVF
hTRbeta	NYRKHHVTHF	WPKLL....M	KVTDLRMIGA	CHASRFL..H	MKVEC..PTE	LLPPLFLEVF
hRARalpha	RKRRPSRPHM	FPKML....M	KITDLRSISA	KGAERVI..T	LKMEI..PGS	M.PPLIQEML
hRARgamma	RRRRPSQPYM	FPRML....M	KITDLRGIST	KGAERAI..T	LKMEI..PGP	M.PPLIREML
hRXRalpha	KHKYPEQPGR	FAKLL....L	RLPALRSIGL	KCLEHLF..F	FKL.I..GDT	PIDTFLMEML
hRXRbeta	KQKYPEQQGR	FAKLL....L	RLPALRSIGL	KCLEHLF..F	FKL.I..GDT	PIDTFLMEML
hPPARalpha	QSNHPDDIFL	FPKLL....Q	KMADLRQLVT	EHAQLVQ..I	IKKTE..SDA	ALHPLLQEIY
hPPARbeta	QANHPDAQYL	FPKLL....Q	KMADLRQLVT	EHAQMMQ..R	IKKTE..TET	SLHPLLQEIY
hPPARgamma	KLNHPESSQL	FAKVL....Q	KMTDLRQIVT	EHVQLLH..V	IKKTE..TDM	SLHPLLQEIY
hVDR	ELWNQKGQQN	LMEFVGGEPS	KKRKRRTSFT	PQAIEVLNTY	FEKNSLPTGQ	EITEIAKELN
hER	GLTLQQQHQR	LAQLL....L	ILSHIRHMSN	KGMEHLY..S	MKC.K..NVV	PLYDLLLEML
hGR	EGNSSQNWQR	FYQLT....K	LLDSMHEVVE	NLLNYCFQTF	LD.KT..MSI	EFPEMLAEII
hPR	QKGVVSSSQR	FYQLT....K	LLDNLHDLVK	QLHLYCLNTF	IQSRA..LSV	EFPEMMSEVI
hMR	PNNSGQSWQR	FYQLT....K	LLDSMHDLVS	DLLEFCFYTF	RESHA..LKV	EFPAMLVEII
hAR	RKNPTSCSRR	FYQLT....K	LLDSVQPIAR	ELHQFTFDLL	IKSHM..VSV	DFPEMMAEII

FIG.3Q

09637132 .081000

DRAFTSMAN	BY	APPROVED O.G. FIG.
	CLASS	SUBCLASS

minimal end site 1025

```
                1021                                                    1071
rTRalpha        EDQEV..... .......... .......... .......... .......... .
hTRalpha        EDQEV..... .......... .......... .......... .......... .
hTRbeta         ED........ .......... .......... .......... .......... .
hRARalpha       ENSEGLDTLS GQPGGGGRDG GGLAPPPGSC SPSLSPSSNR SSPATHSP.. .
hRARgamma       ENPEMFEDDS SQPGPHPNAS SEDEVPGGQG KGGLKSPA.. .......... .
hRXRalpha       EAPHQMT... .......... .......... .......... .......... .
hRXRbeta        EAPHQLA... .......... .......... .......... .......... .
hPPARalpha      RDMY...... .......... .......... .......... .......... .
hPPARbeta       KDMY...... .......... .......... .......... .......... .
hPPARgamma      KDLY...... .......... .......... .......... .......... .
hVDR            YDREVVRVWF CNRRQTLKNT SKINVFQSQ. .......... .......... .
hER             DAHRLHAPTS RGGASVEETD QSHLATAGST SSHSLQKYYI TGEAEGFPAT V
hGR             TNQIPKYSNG NIKKLLFHQK .......... .......... .......... .
hPR             AAQLPKILAG MVKPLLFHKK .......... .......... .......... .
hMR             SDQLPKVESG NAKPLYFHRK .......... .......... .......... .
hAR             SVQVPKILSG KVKPIYFHTQ .......... .......... .......... .

socr:<5>
```

FIG.3R

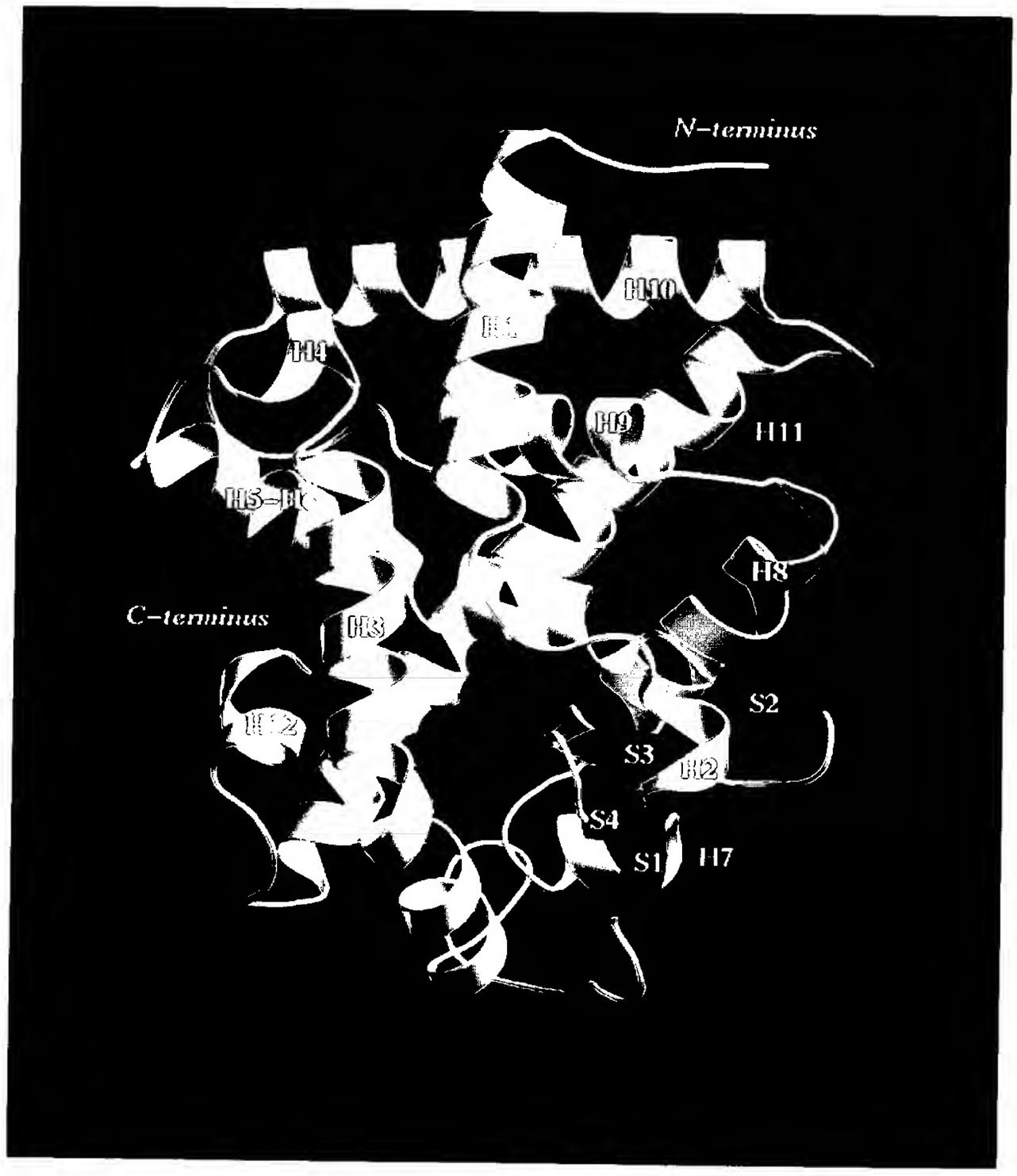
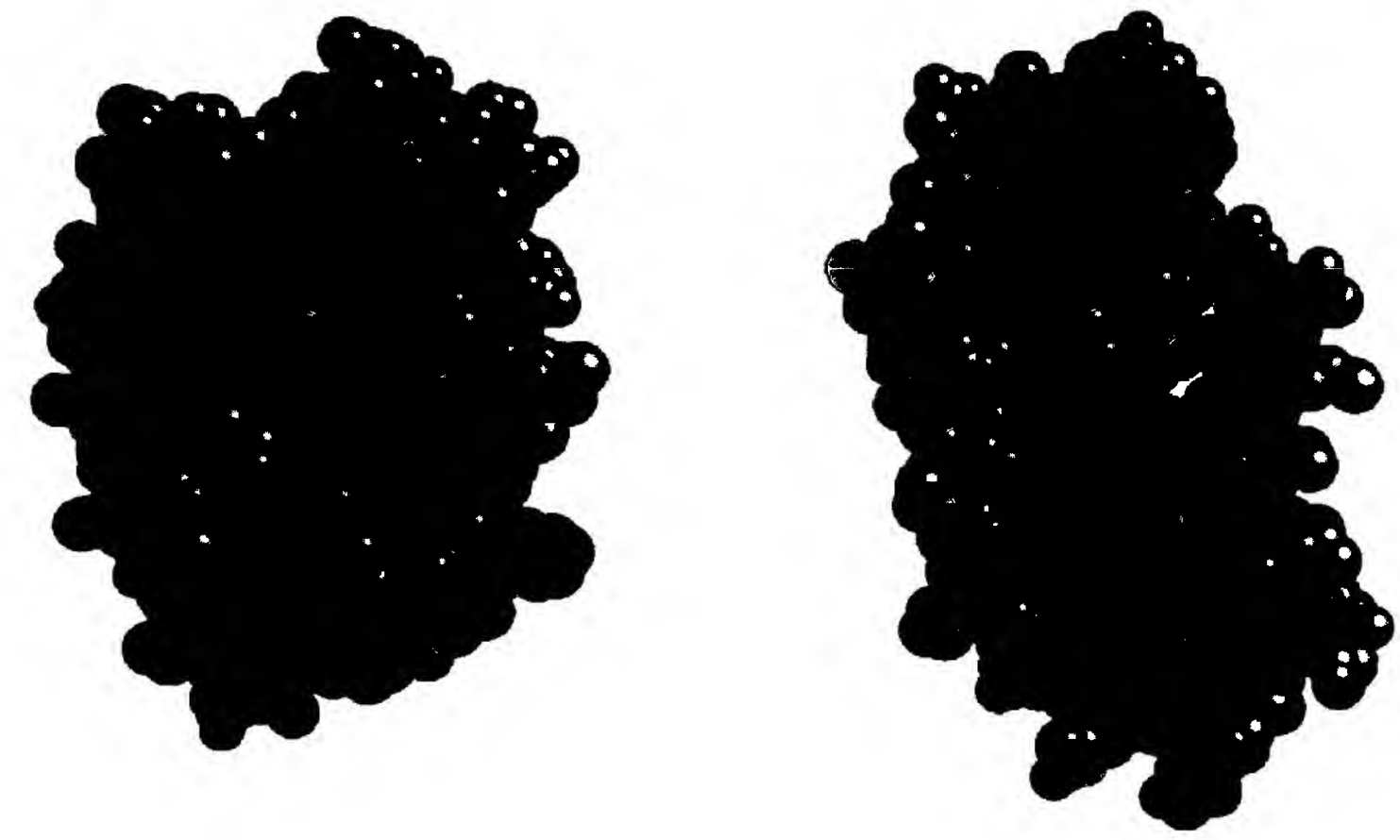

N–terminus
H10
H14
H9
H11
H5–H6
H8
C–terminus
H3
H12
S2
S3
H2
S4
S1
H7

FIG. 4

FIG. 5



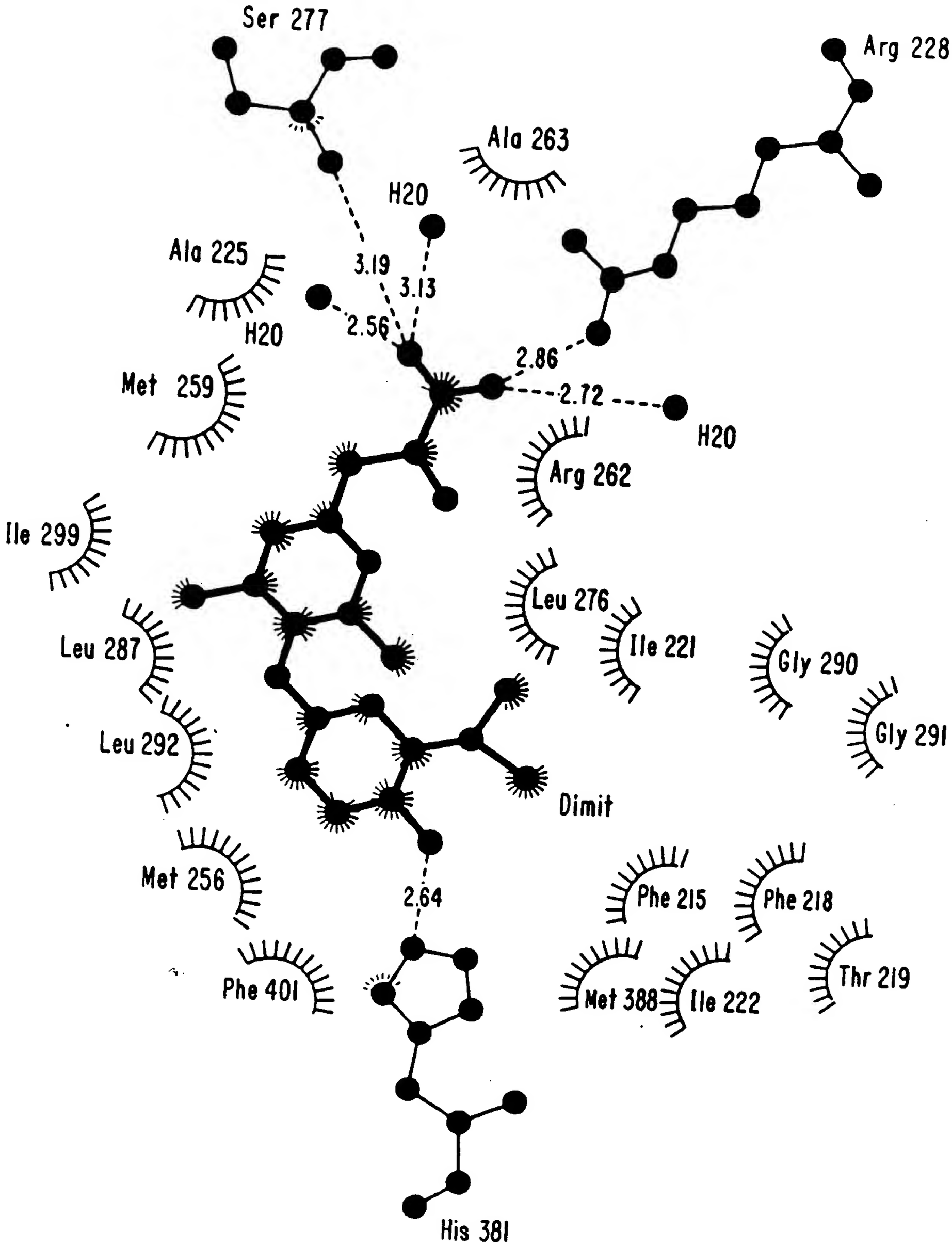


FIG.6

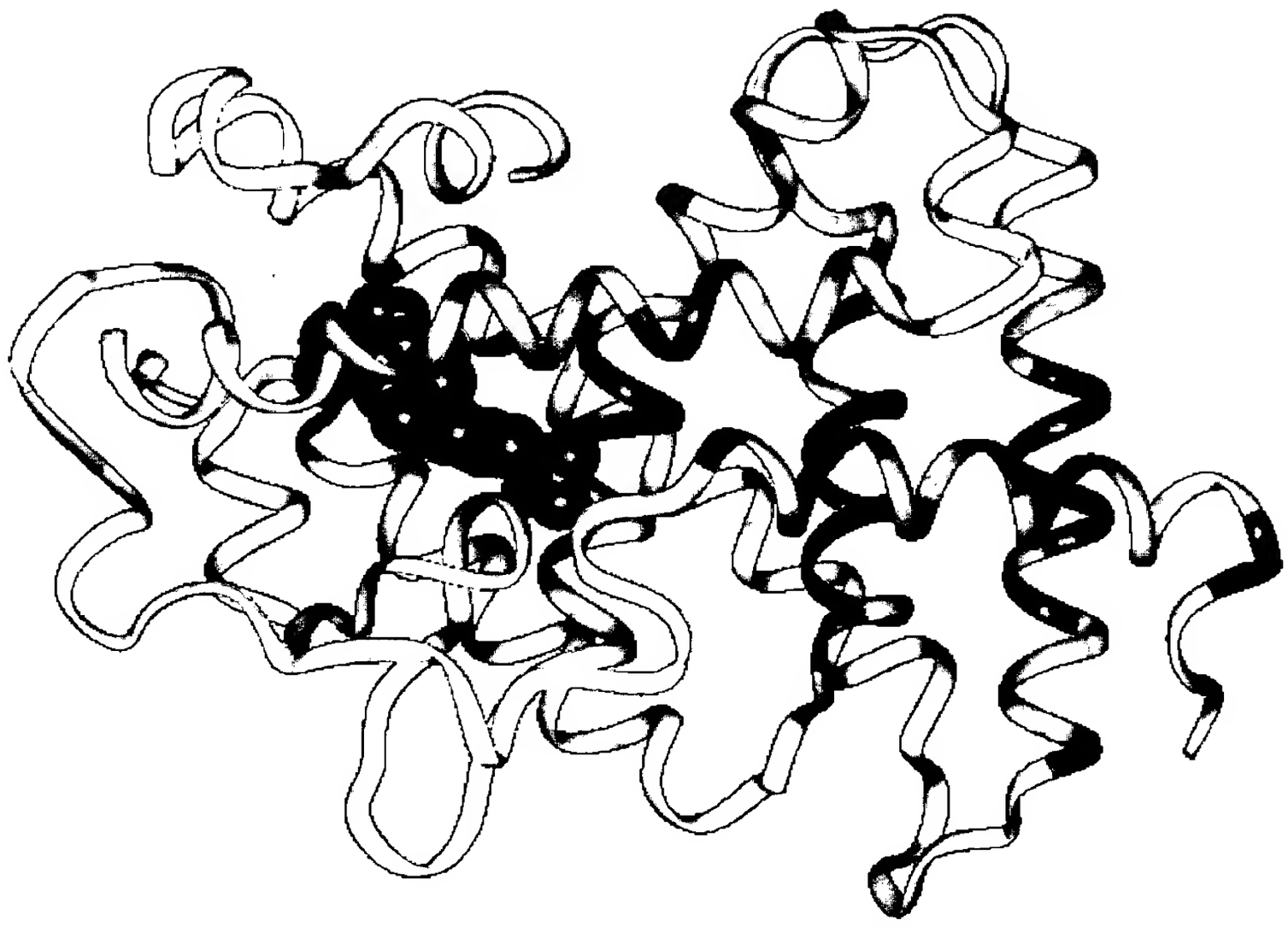


FIG. 7

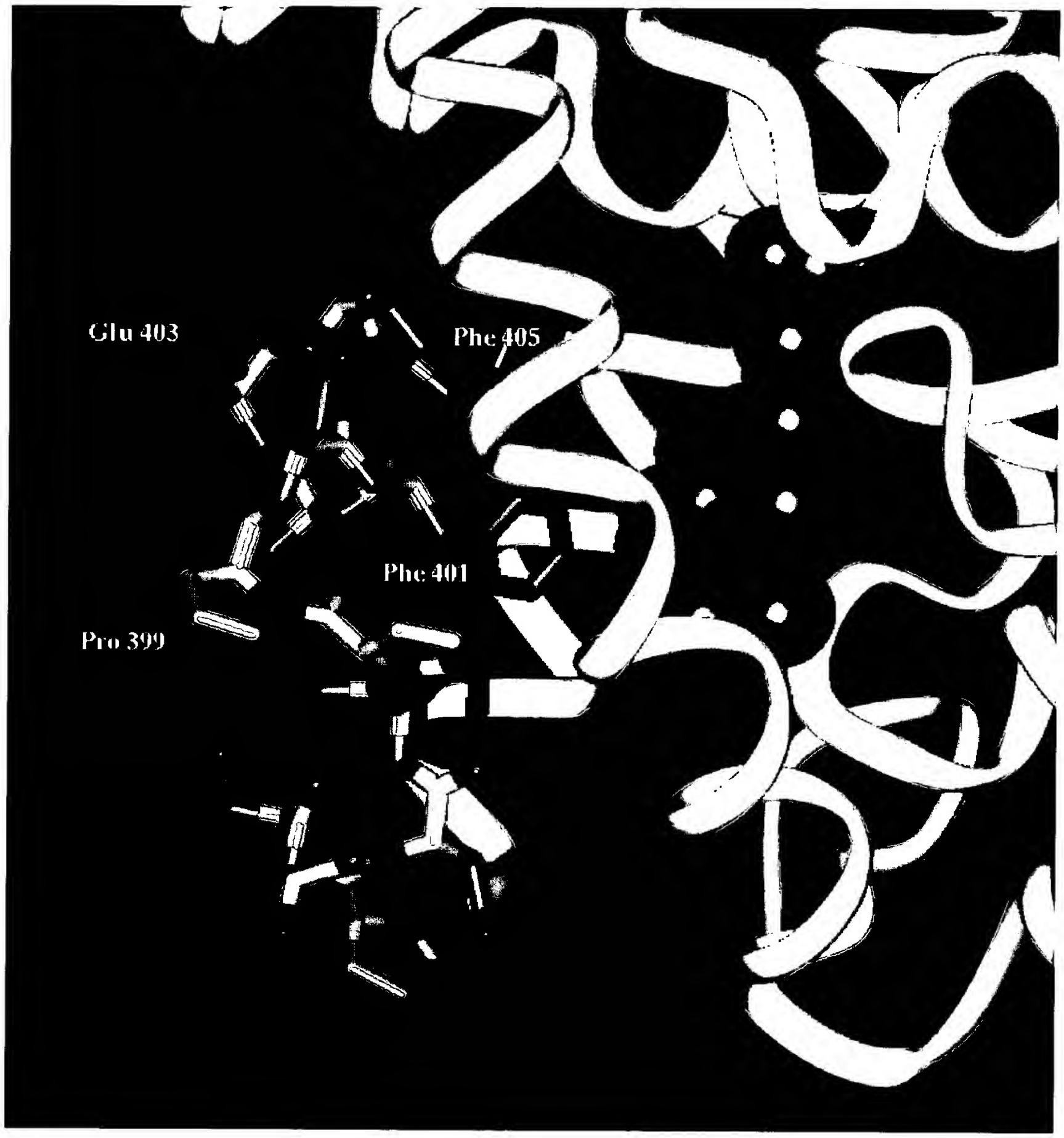


FIG. 8

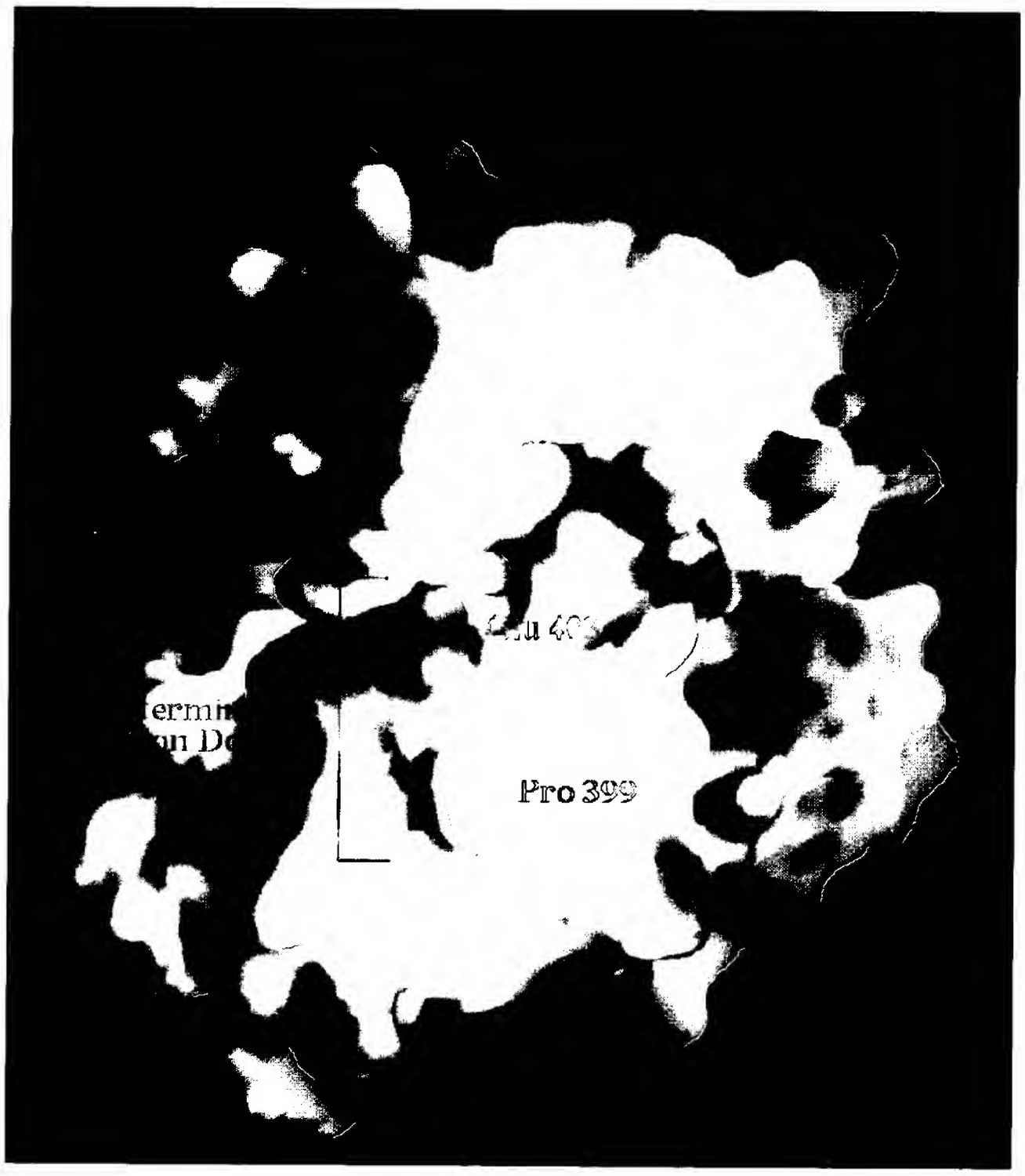
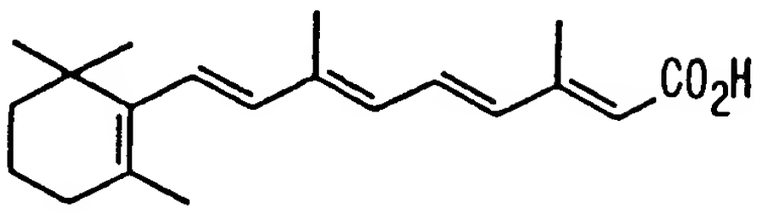


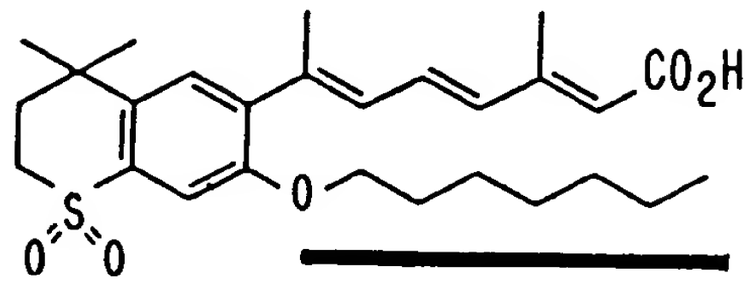
FIG. 9

AGONISTS

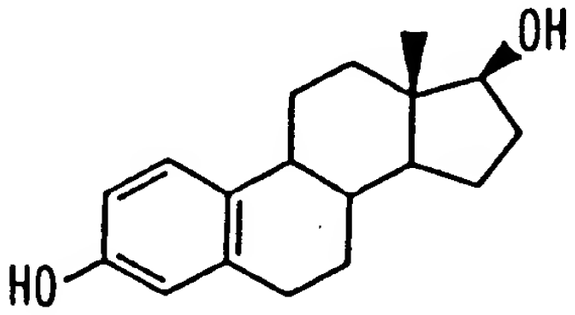


Retinoic Acid

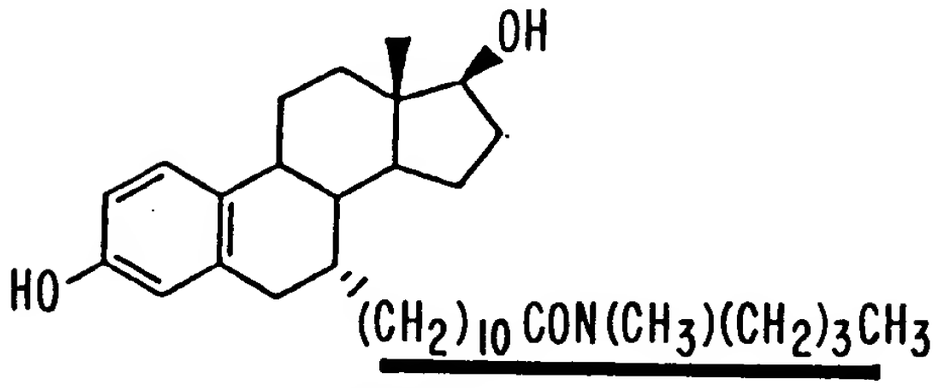
ANTAGONISTS



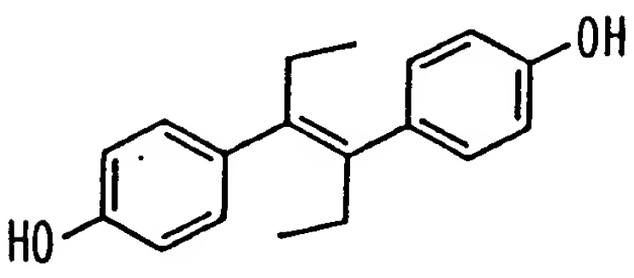
RO 46-8515



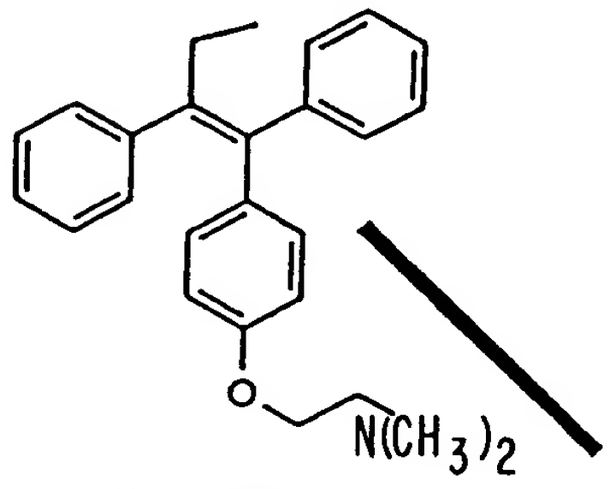
Estradiol



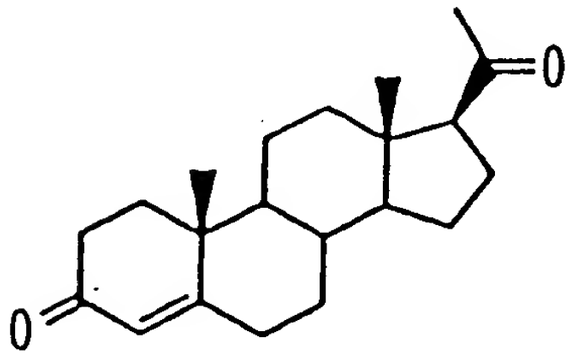
ICI 164384



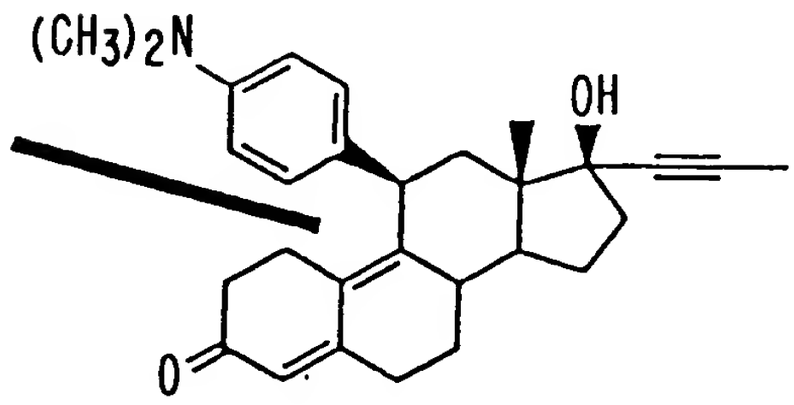
Diethylstilbestrol



Tamoxifen



Progesterone

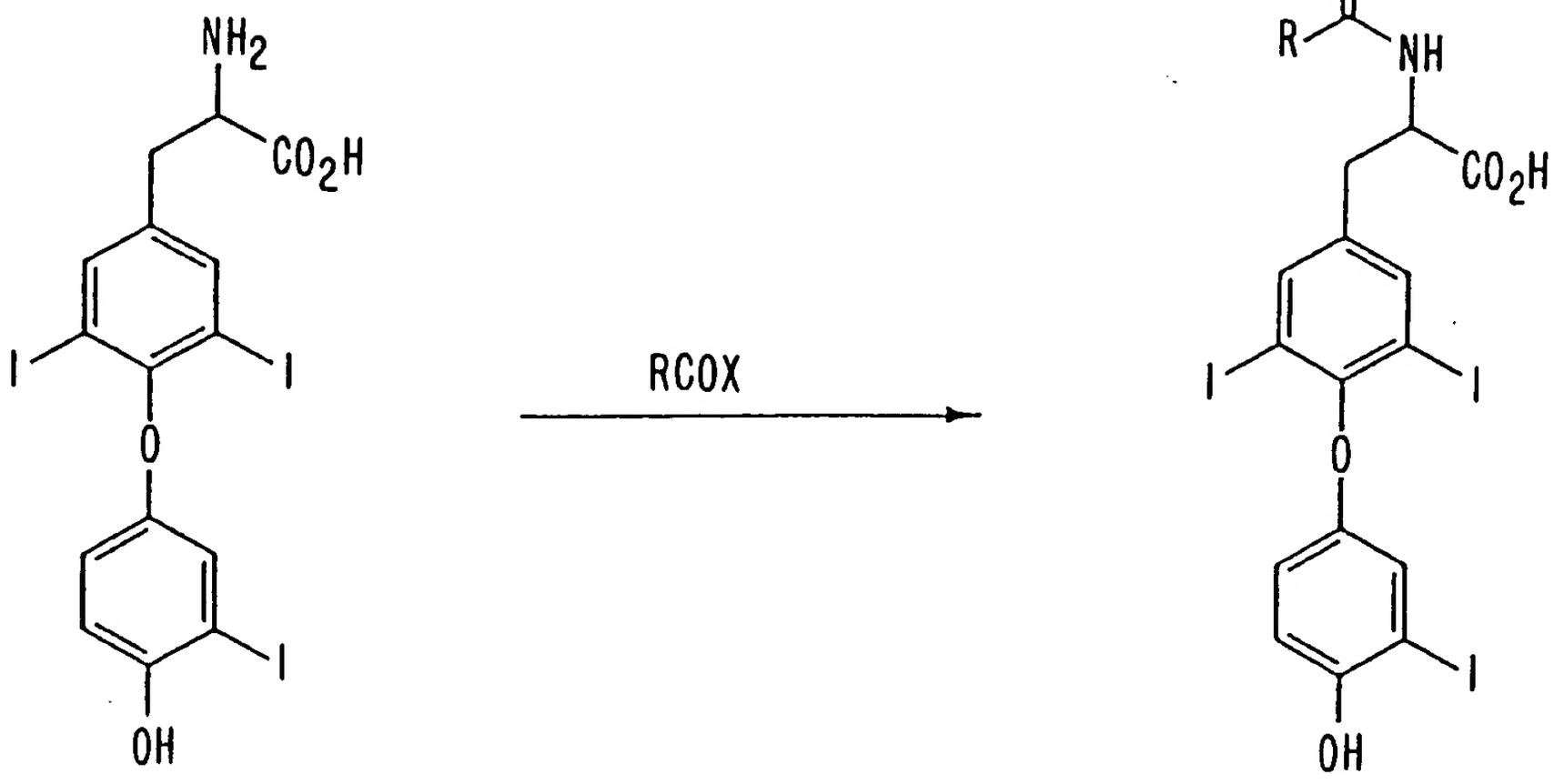


RU 486

FIG. 10

shows position of extension group

APPROVED BY DRAFTSMAN	O G. FIG.	
	CLASS	SUBCLASS



Compound	RCOX
TS1	Ph_2CHCO_2NHS
TS2	$C_{16}H_{33}CO_2NHS$
TS3	FMOC-Cl
TS4	$tBOC_2O$
TS5	$tBOC_2O$

FIG. 11

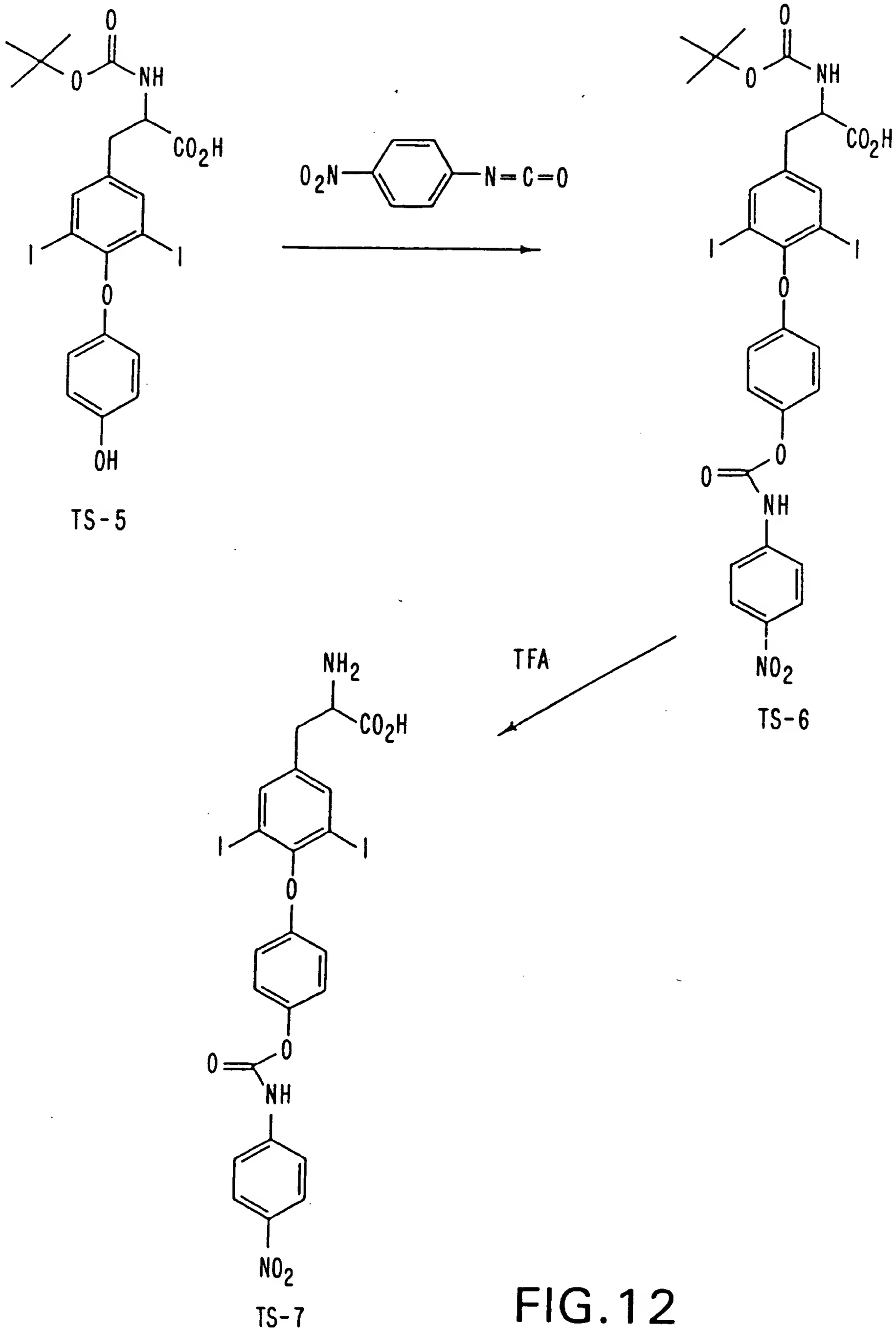
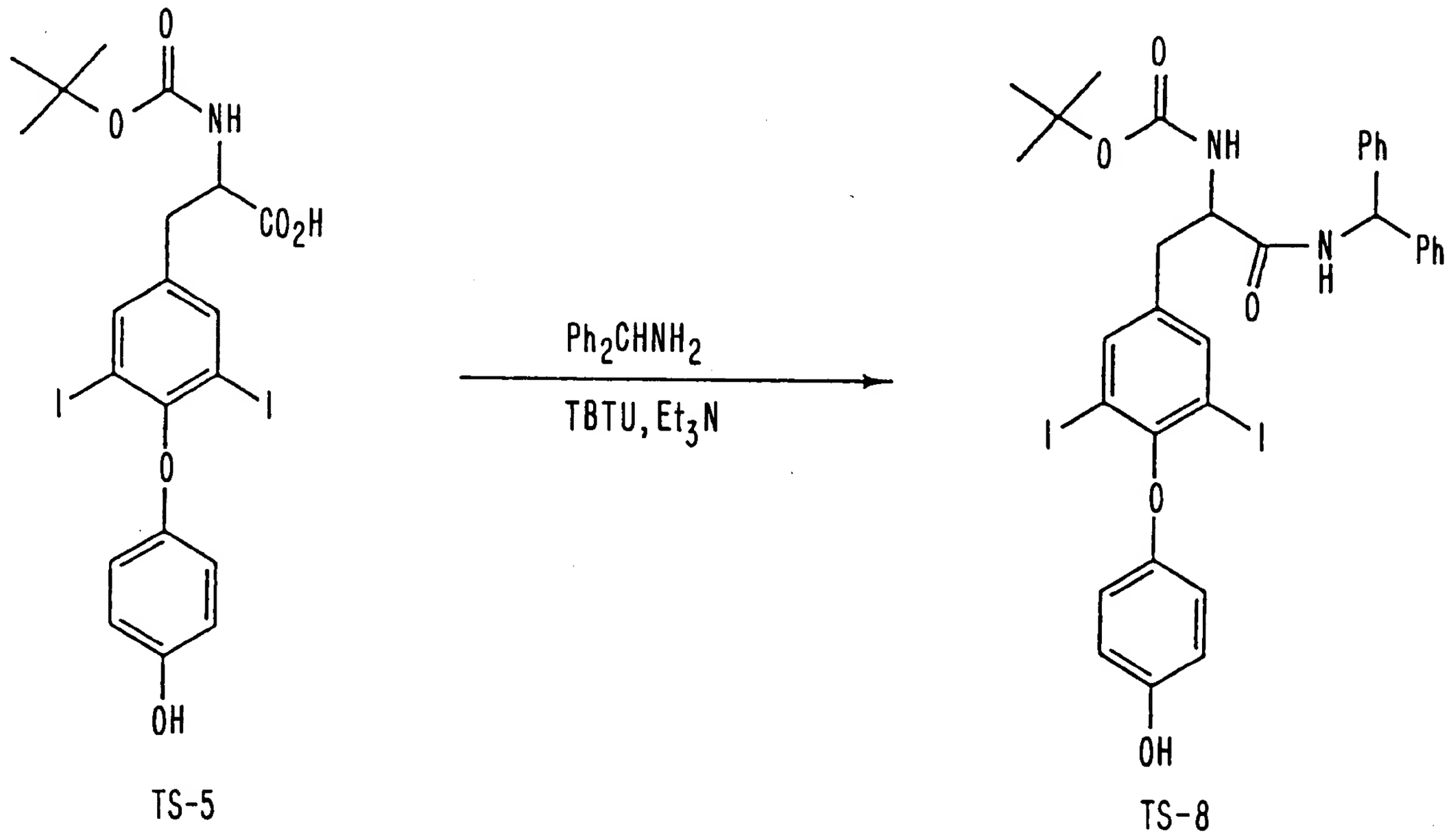


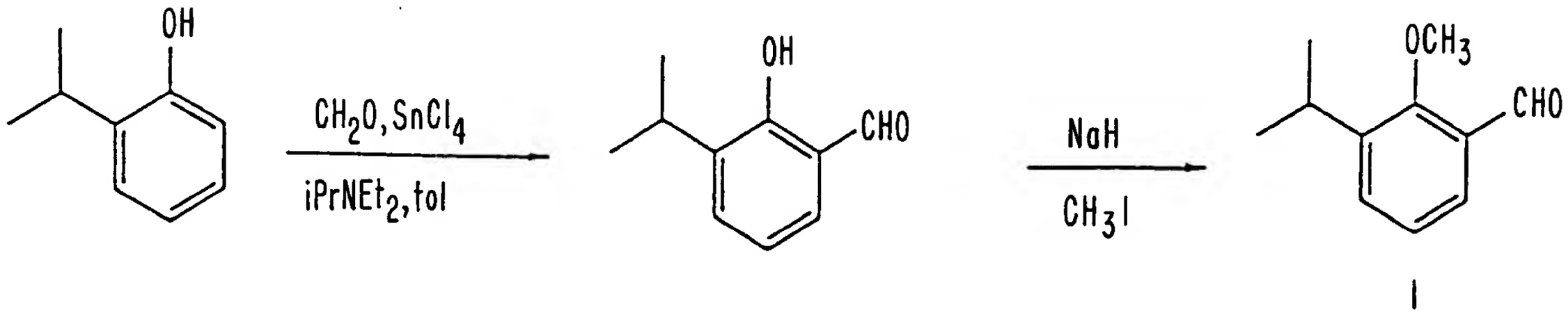
FIG.12



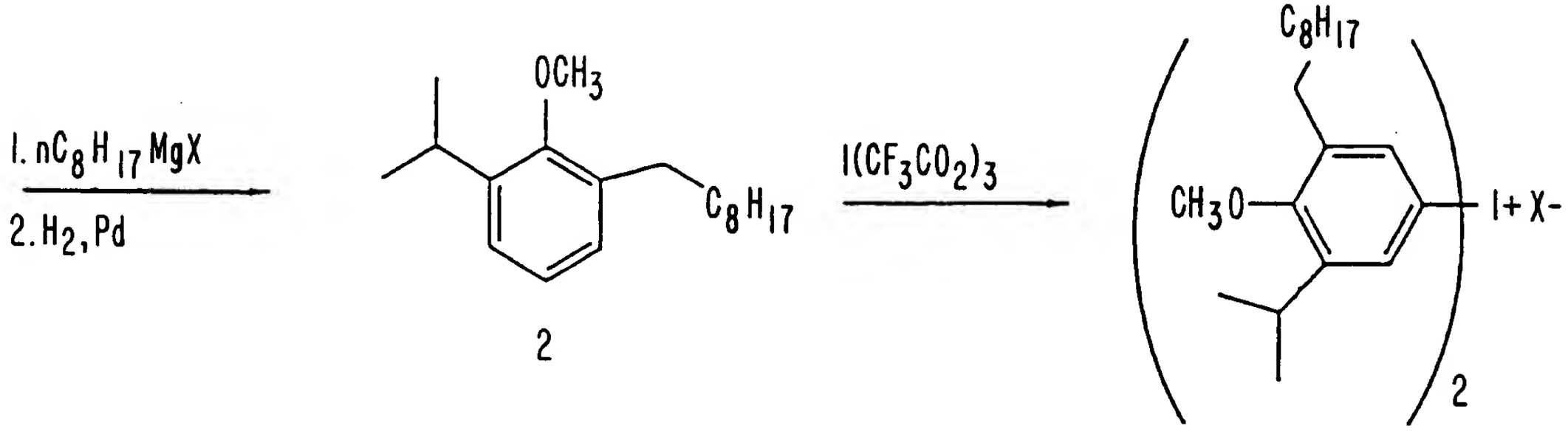
TS-5

TS-8

FIG.13

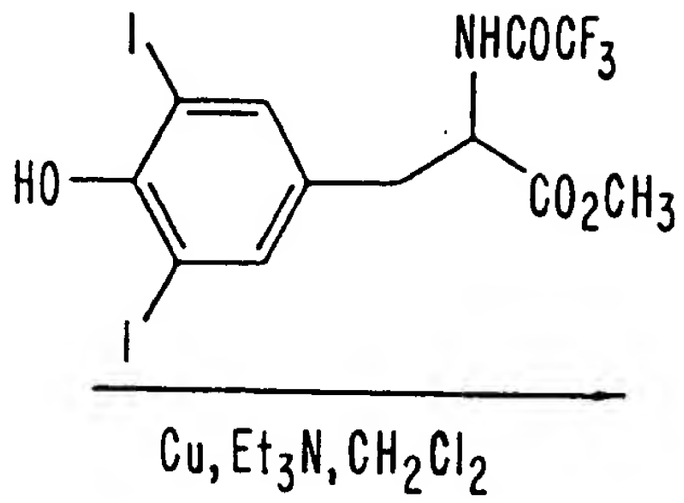


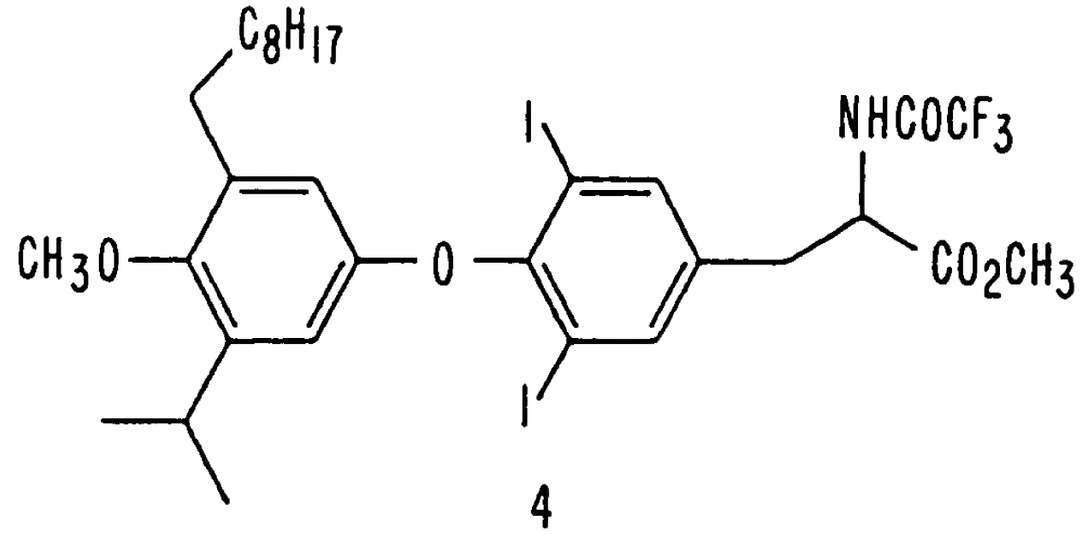
1



3

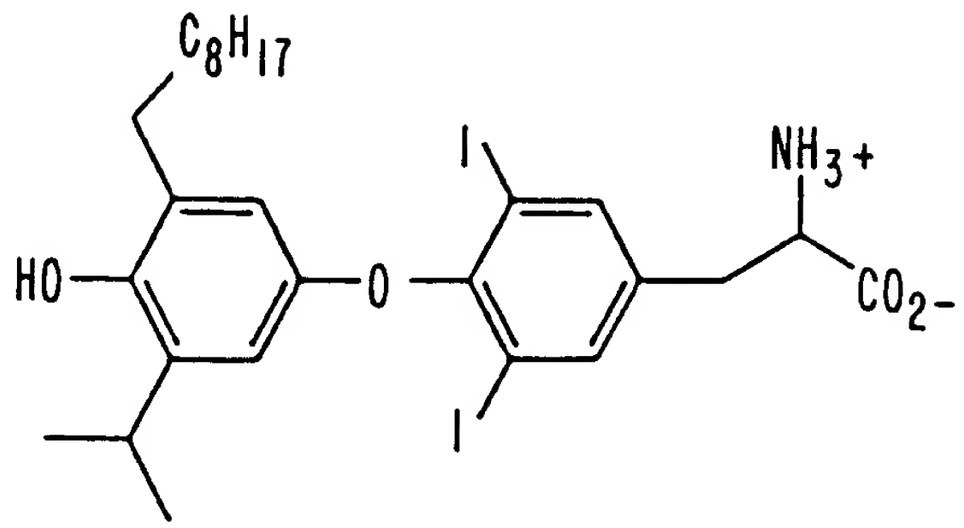
FIG. 14A





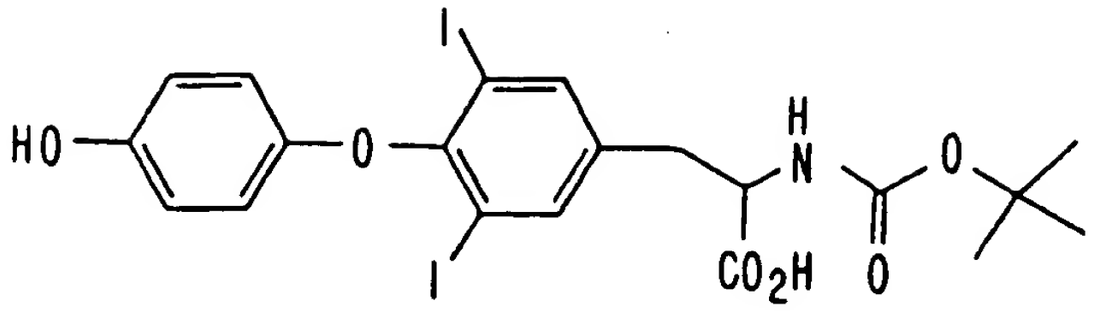
4

HBr, AcOH

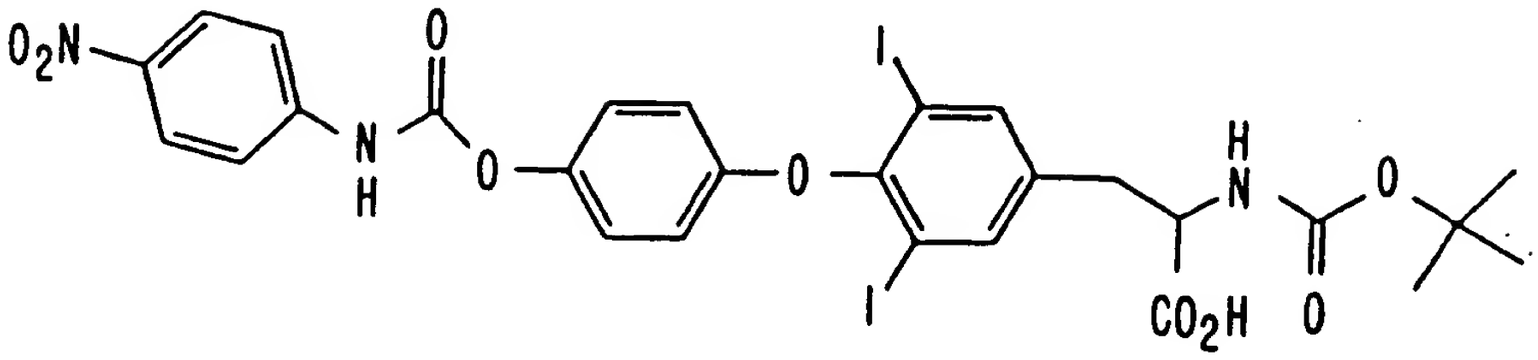


TS-10

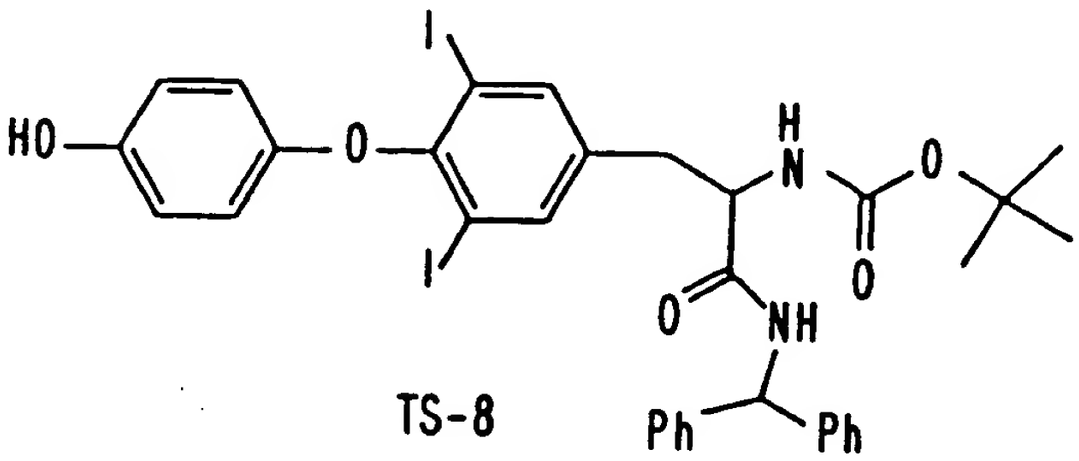
FIG.14B



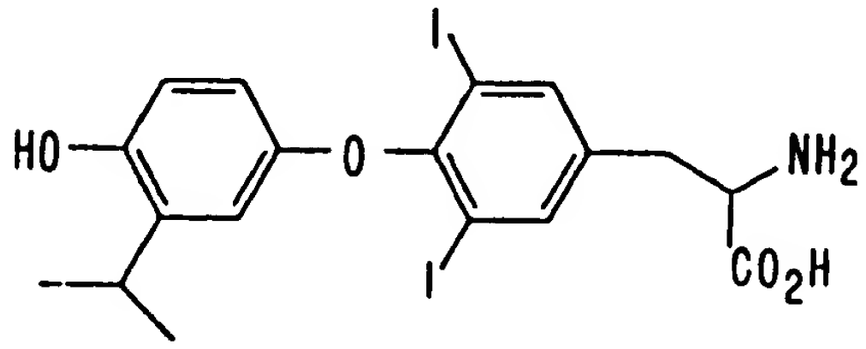
TS-5



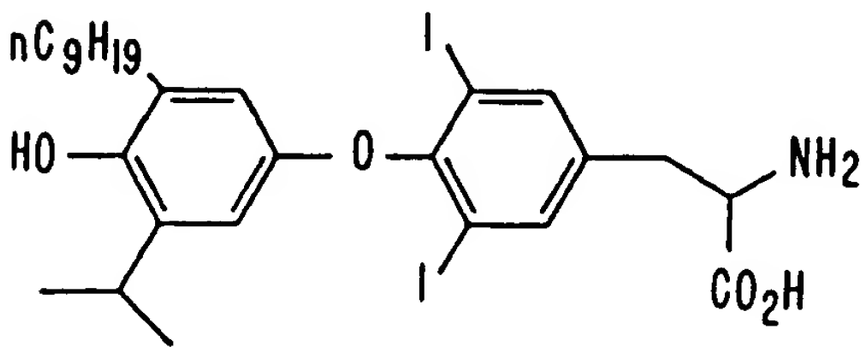
TS-6



TS-8



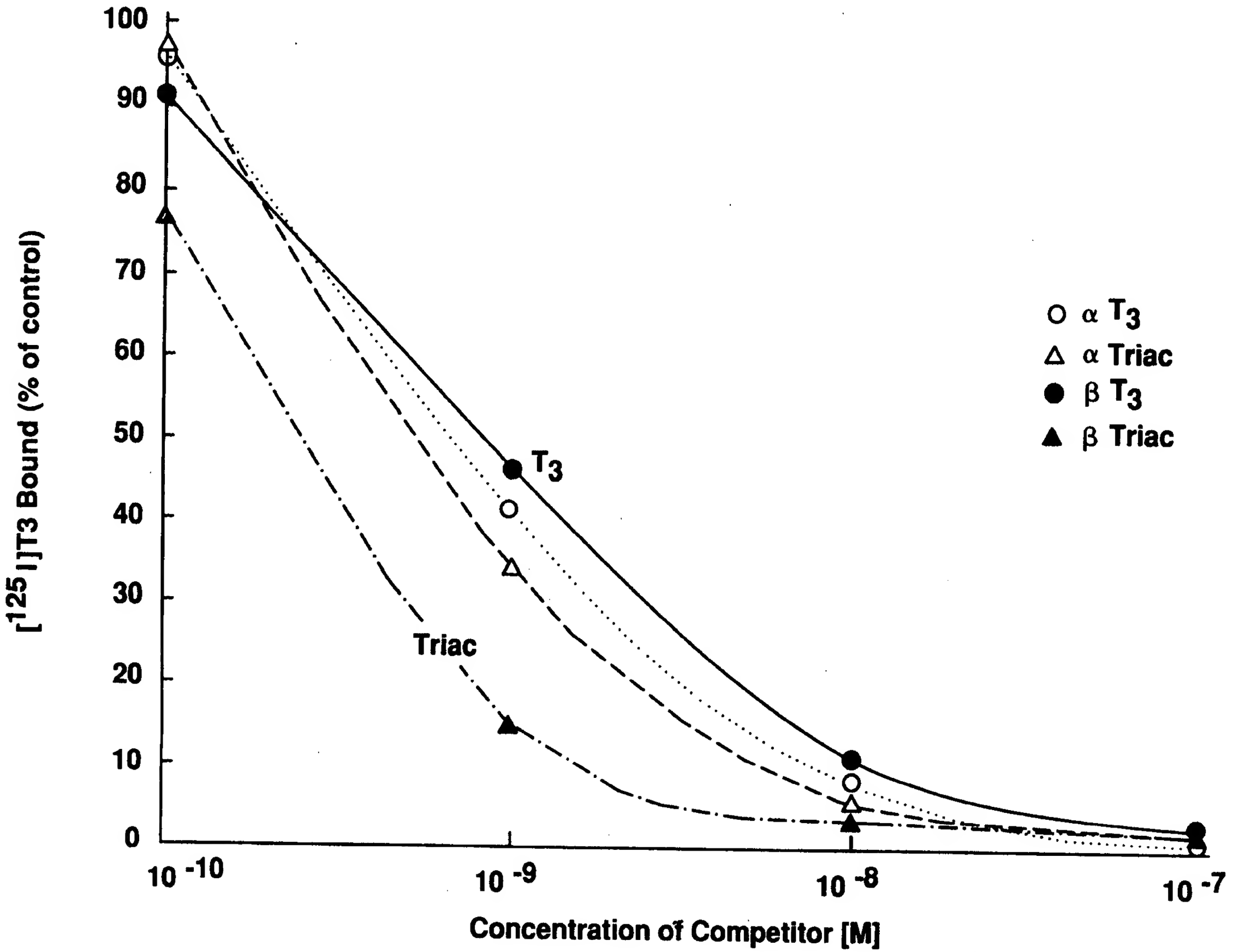
TS-9



TS-10

FIG. 15

FIG.16


100
90
80
70
60
50
40
30
20
10
0
[125I]T3 Bound (% of control)
T3
Triac
10 -10
10 -9
10 -8
10 -7
Concentration of Competitor [M]
α T3
α Triac
β T3
β Triac

APPROVED BY DRAFTSMAN	C.G. FIG.	
	CLASS	SUBCLASS

FIG.17A

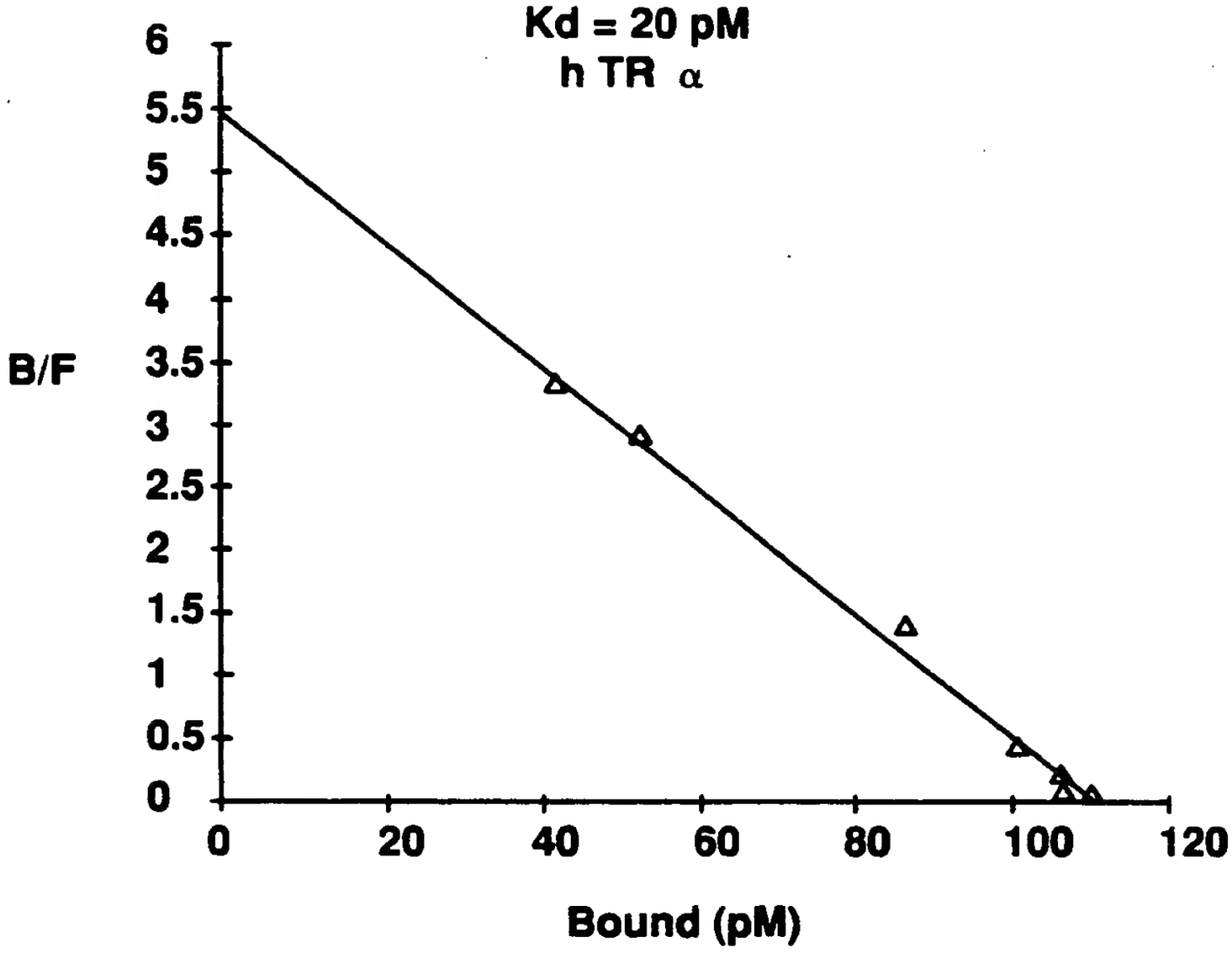
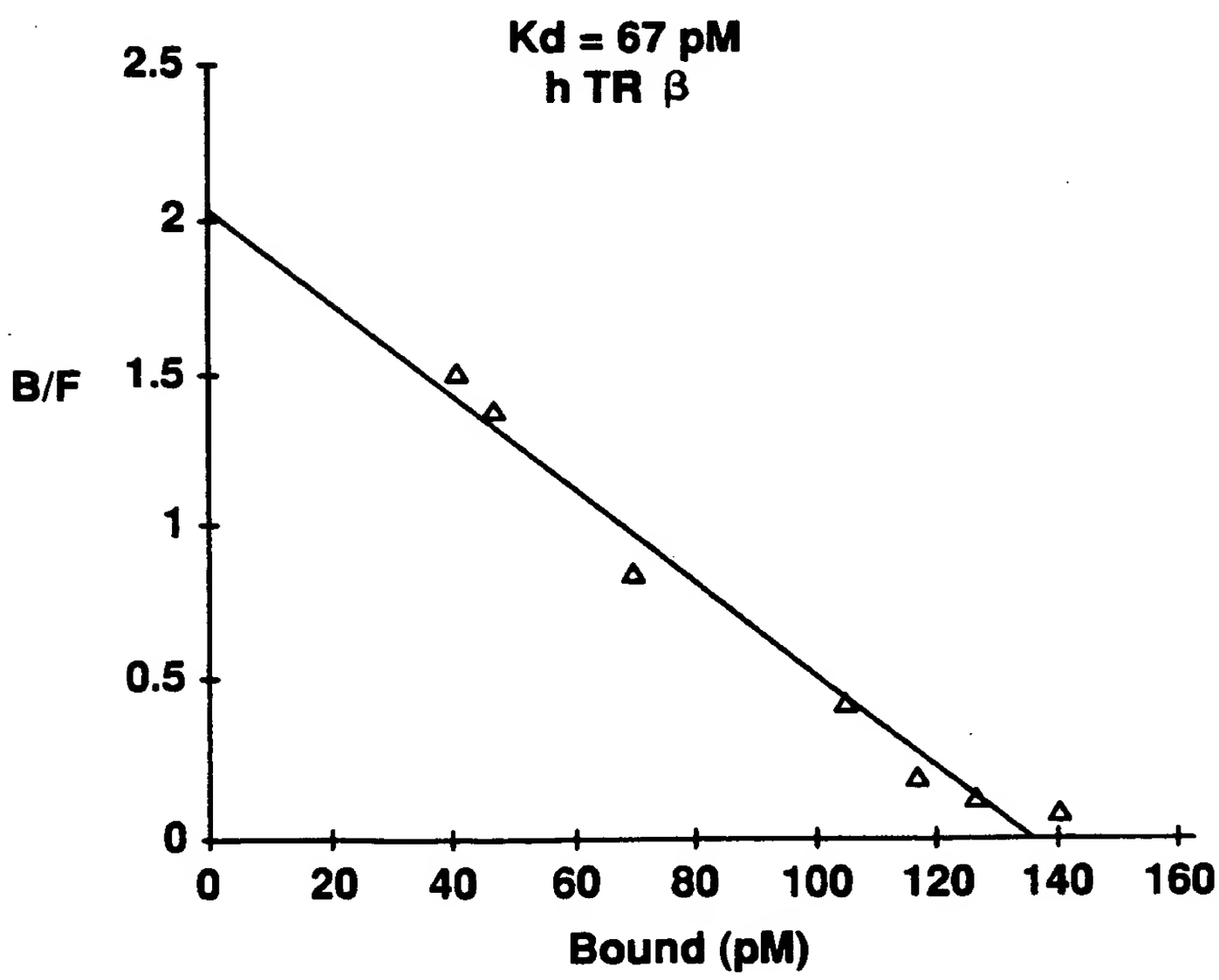


FIG.17B



APPROVED BY DRAFTSMAN	O G. FIG.	
	CLASS	SUBCLASS

FIG.18

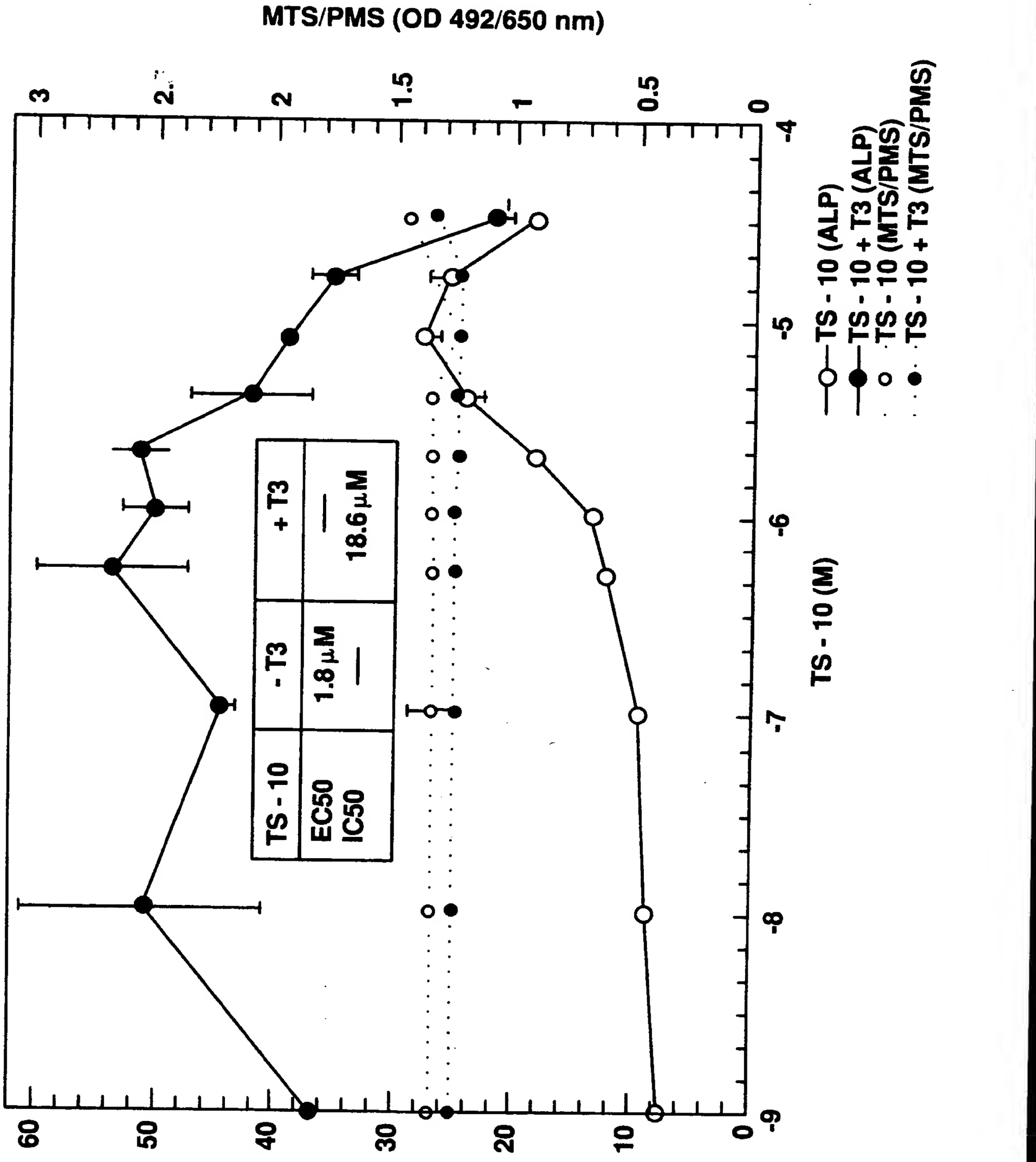


FIG.19

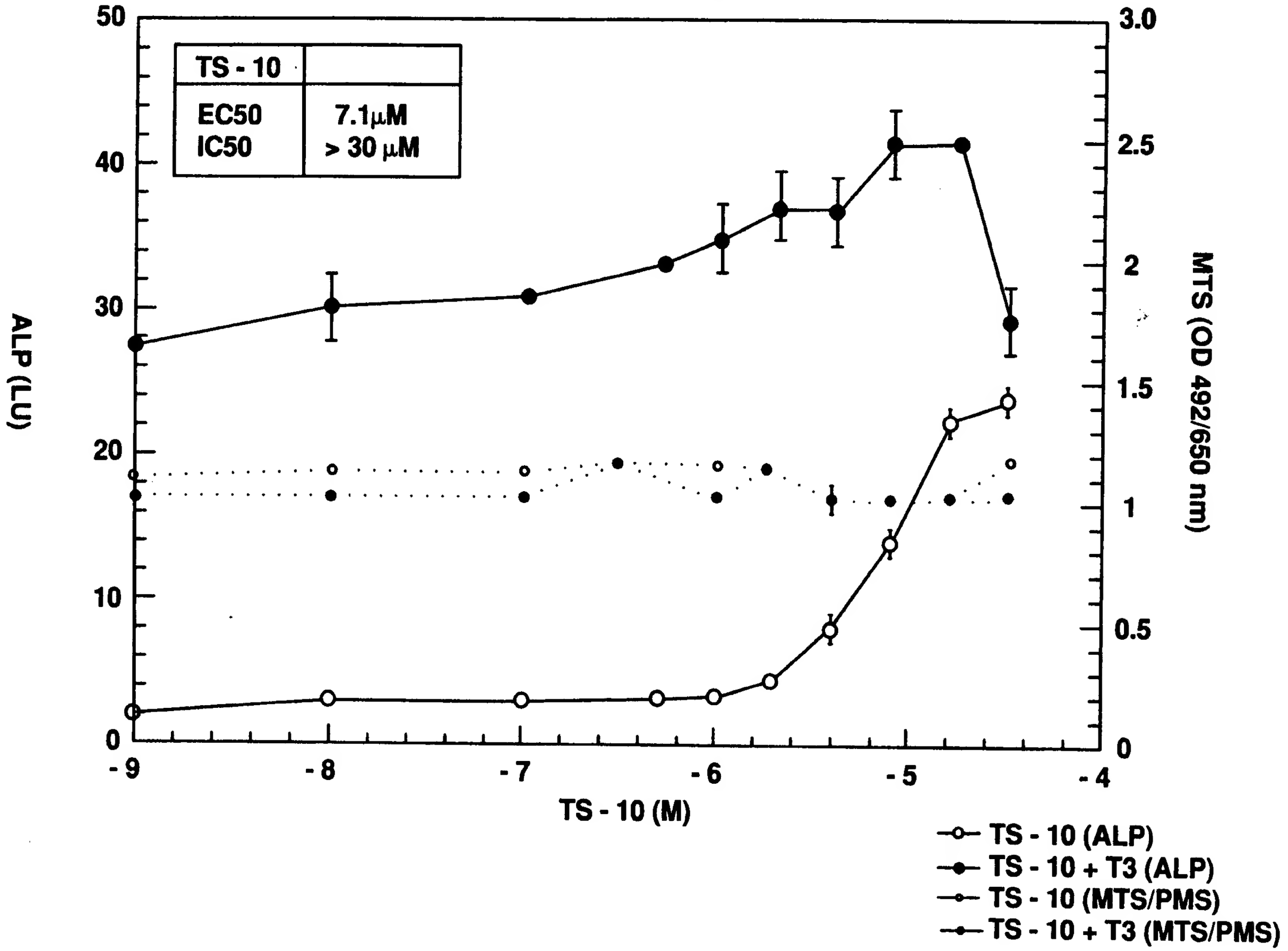
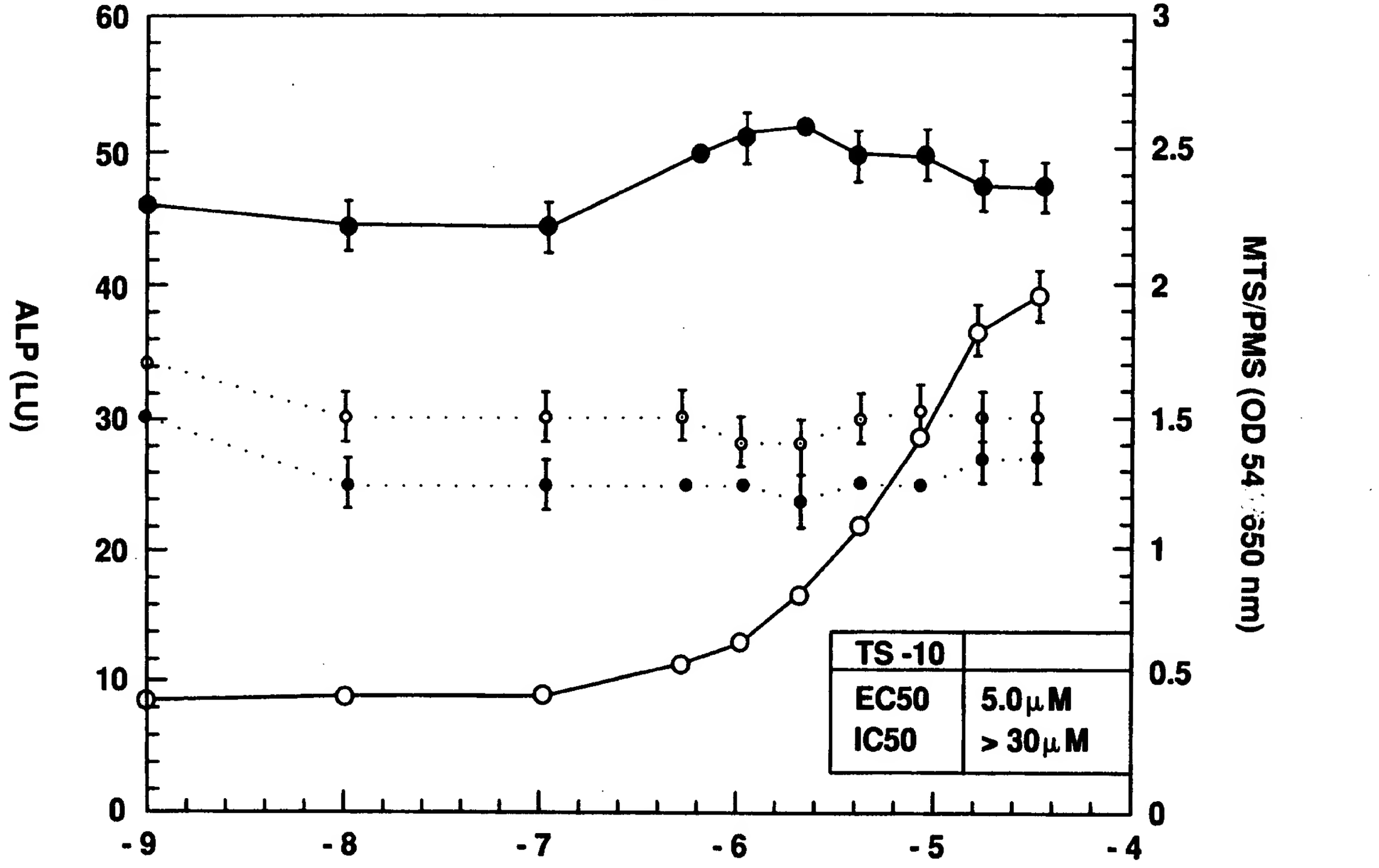


FIG.20



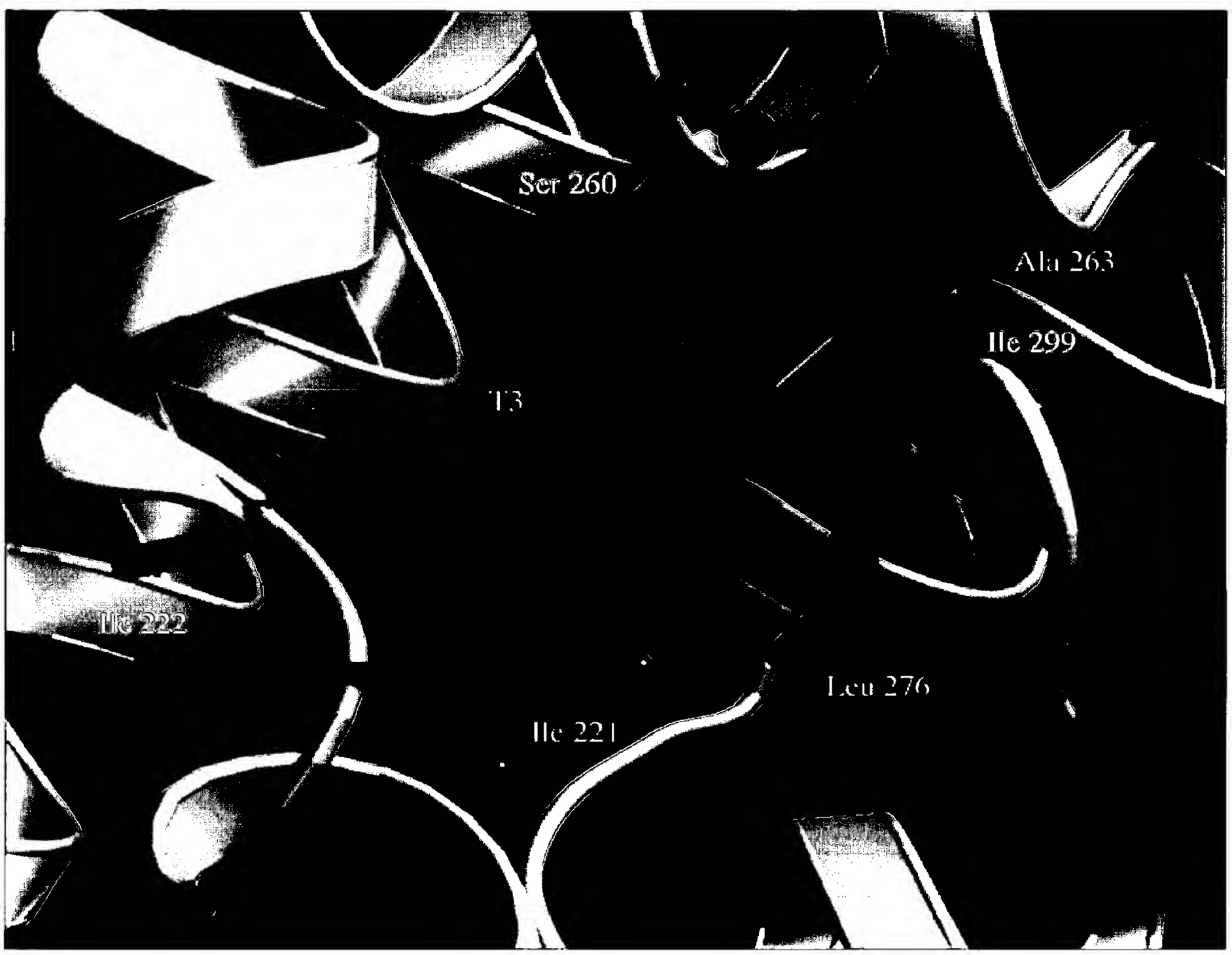


FIG. 21

FIG. 22


Gln 320
Thr 178
Arg 262
Asn 179
HOH
504
HOH 503
Arg 266
Arg 228
HOH 502
Ser 277
T3

FIG. 23

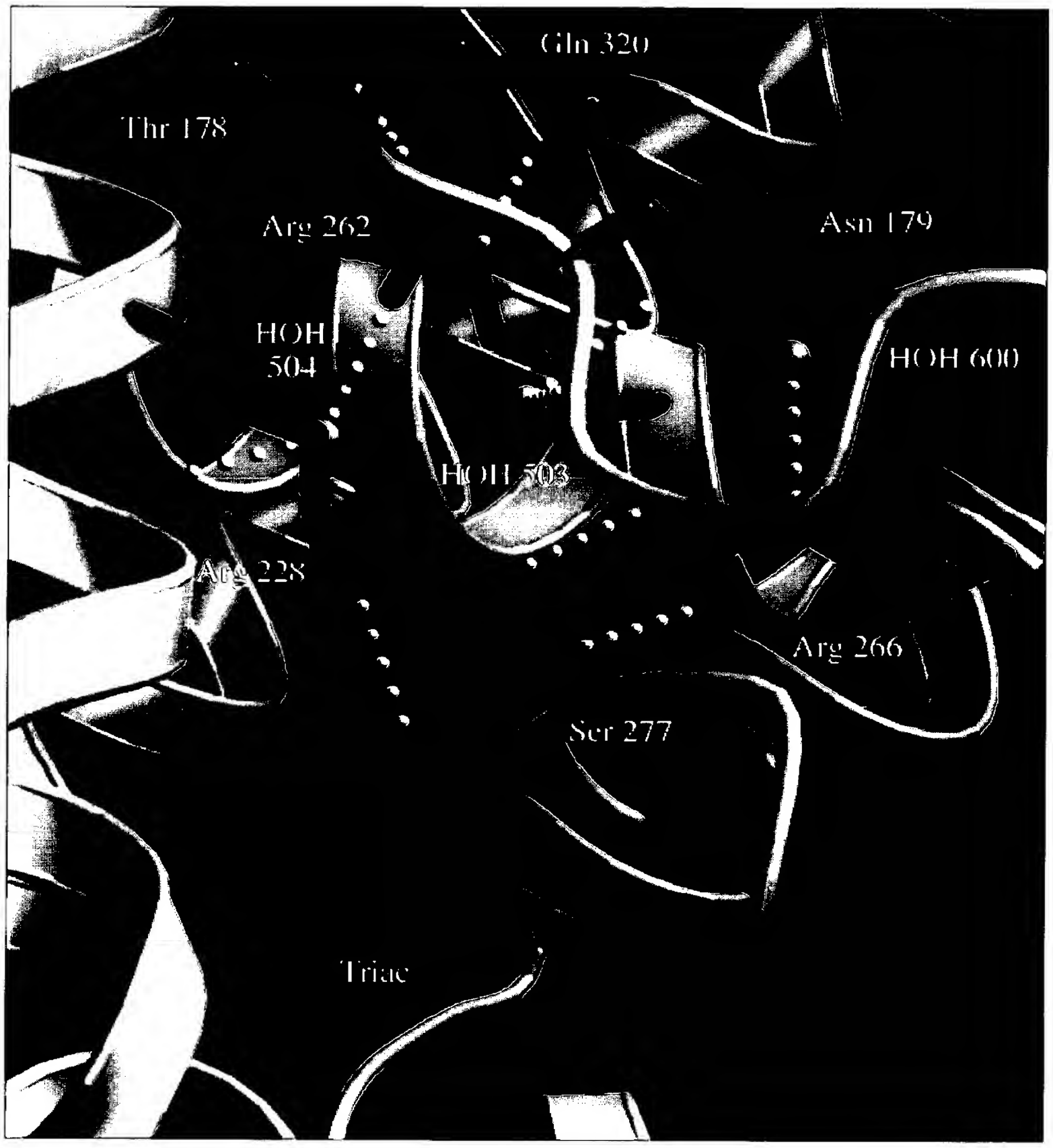

Gln 320
Thr 178
Arg 262
Asn 179
HOH
504
HOH 600
HOH 503
Arg 228
Arg 266
Ser 277
Triac

FIG. 24

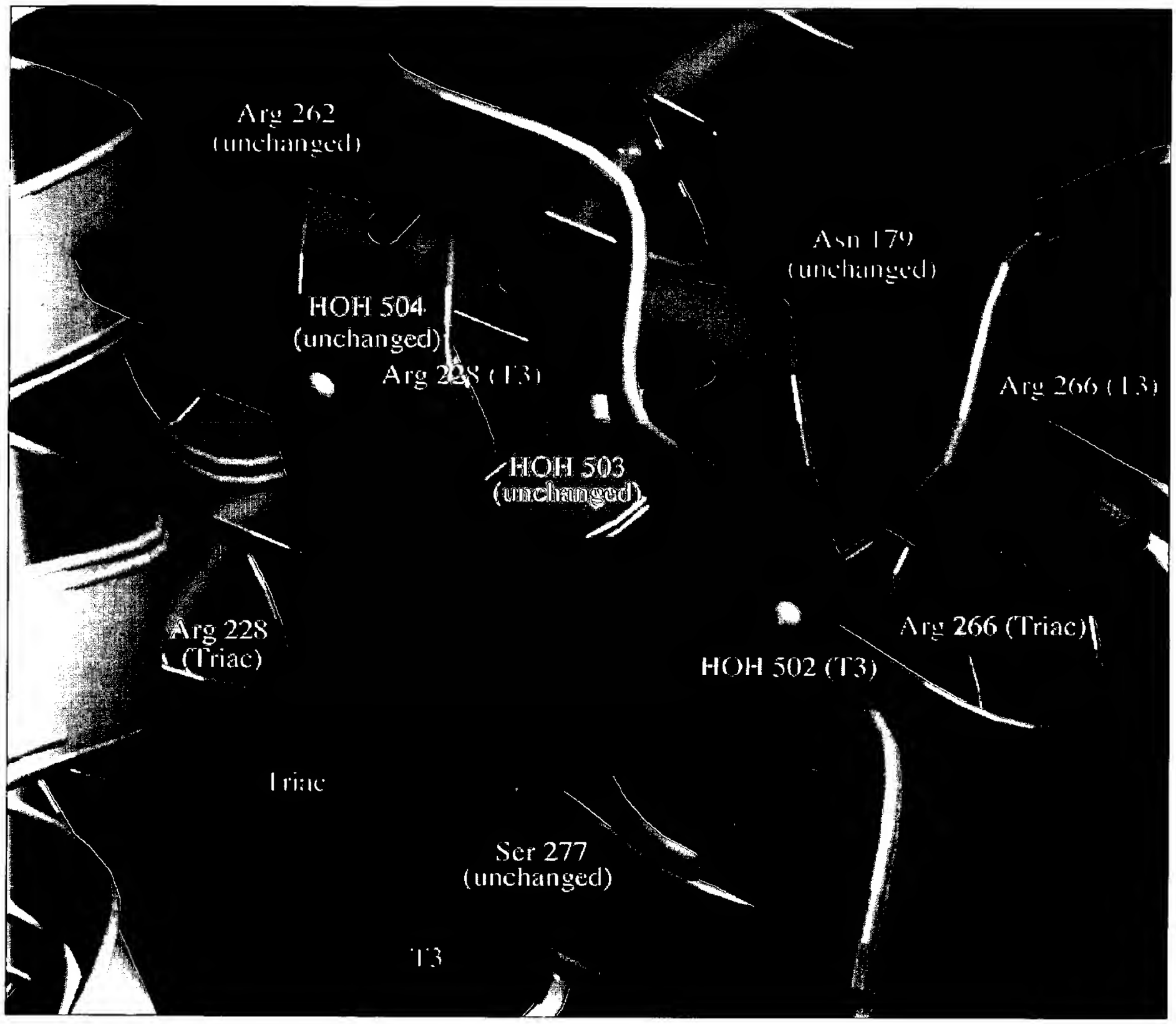

Arg 262
(unchanged)
HOH 504
(unchanged)
Arg 228 (T3)
HOH 503
(unchanged)
Arg 228
(Triac)
Asn 179
(unchanged)
Arg 266 (T3)
Arg 266 (Triac)
HOH 502 (T3)
Triac
Ser 277
(unchanged)
T3

FIG. 25

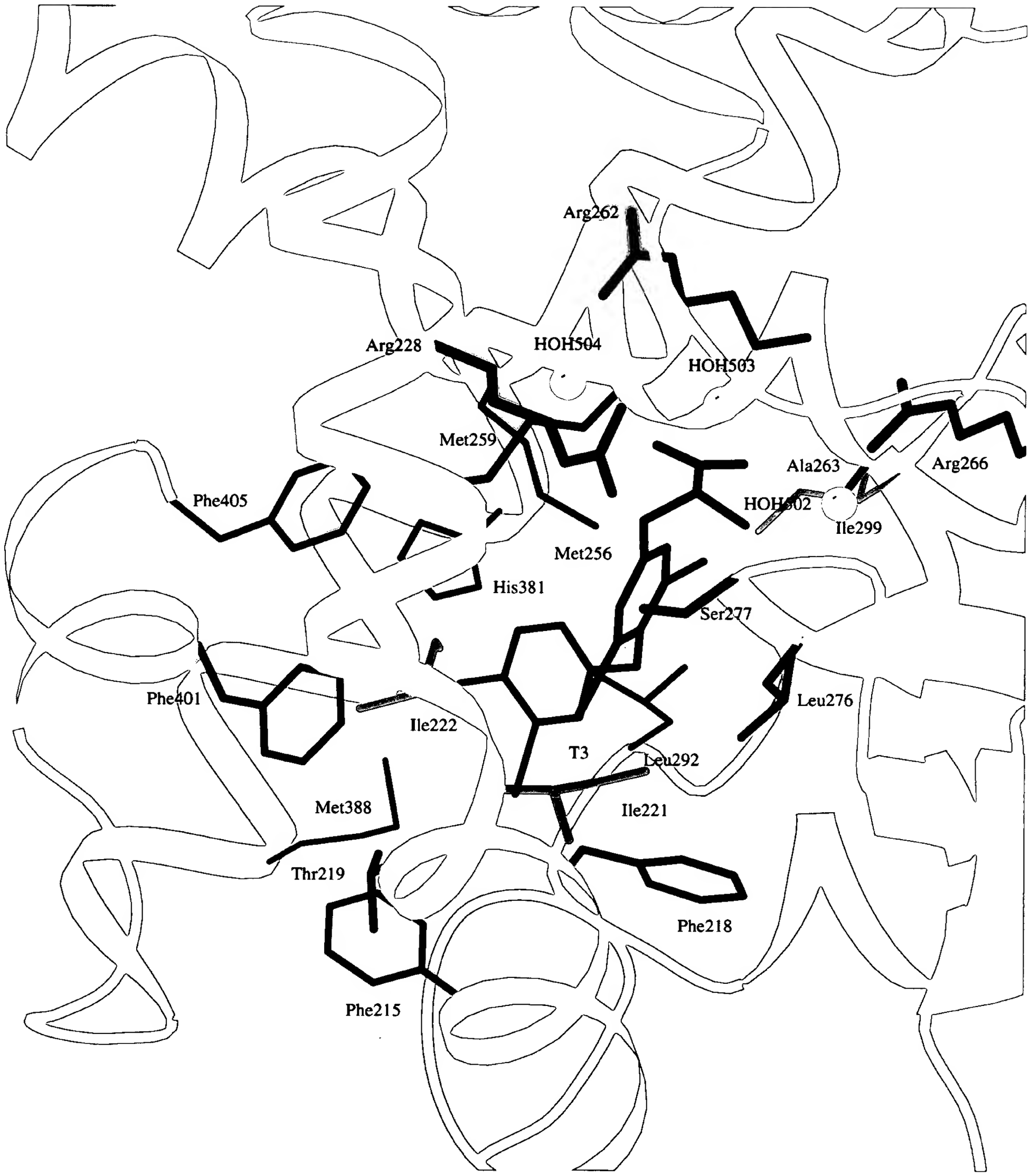


FIG. 26A

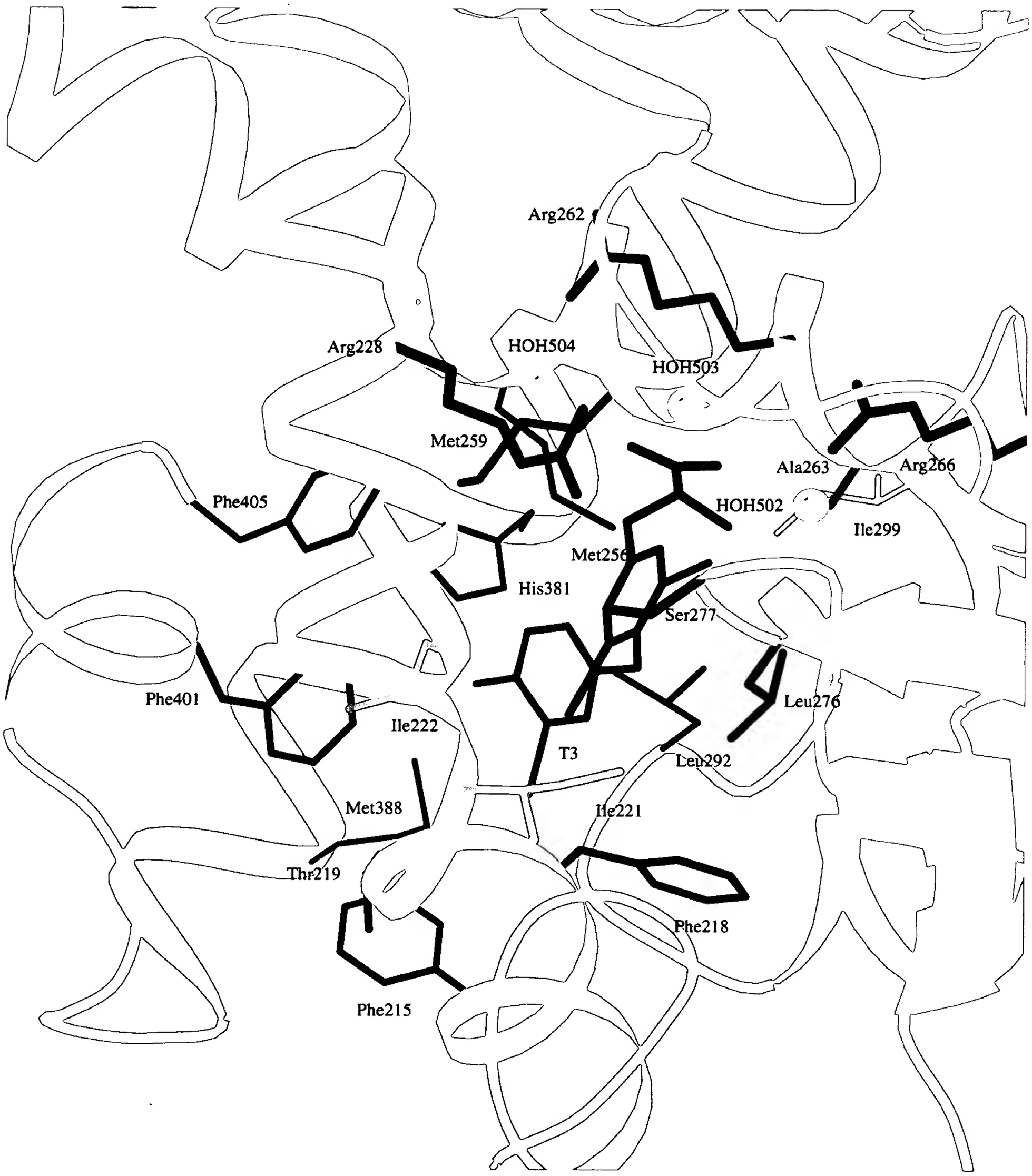

Arg262
Arg228
HOH504
HOH503
Met259
Ala263
Arg266
Phe405
HOH502
Ile299
Met256
His381
Ser277
Phe401
Leu276
Ile222
T3
Leu292
Met388
Ile221
Thr219
Phe218
Phe215

FIG. 26B

Thyroid Hormone Receptor Beta with GC1

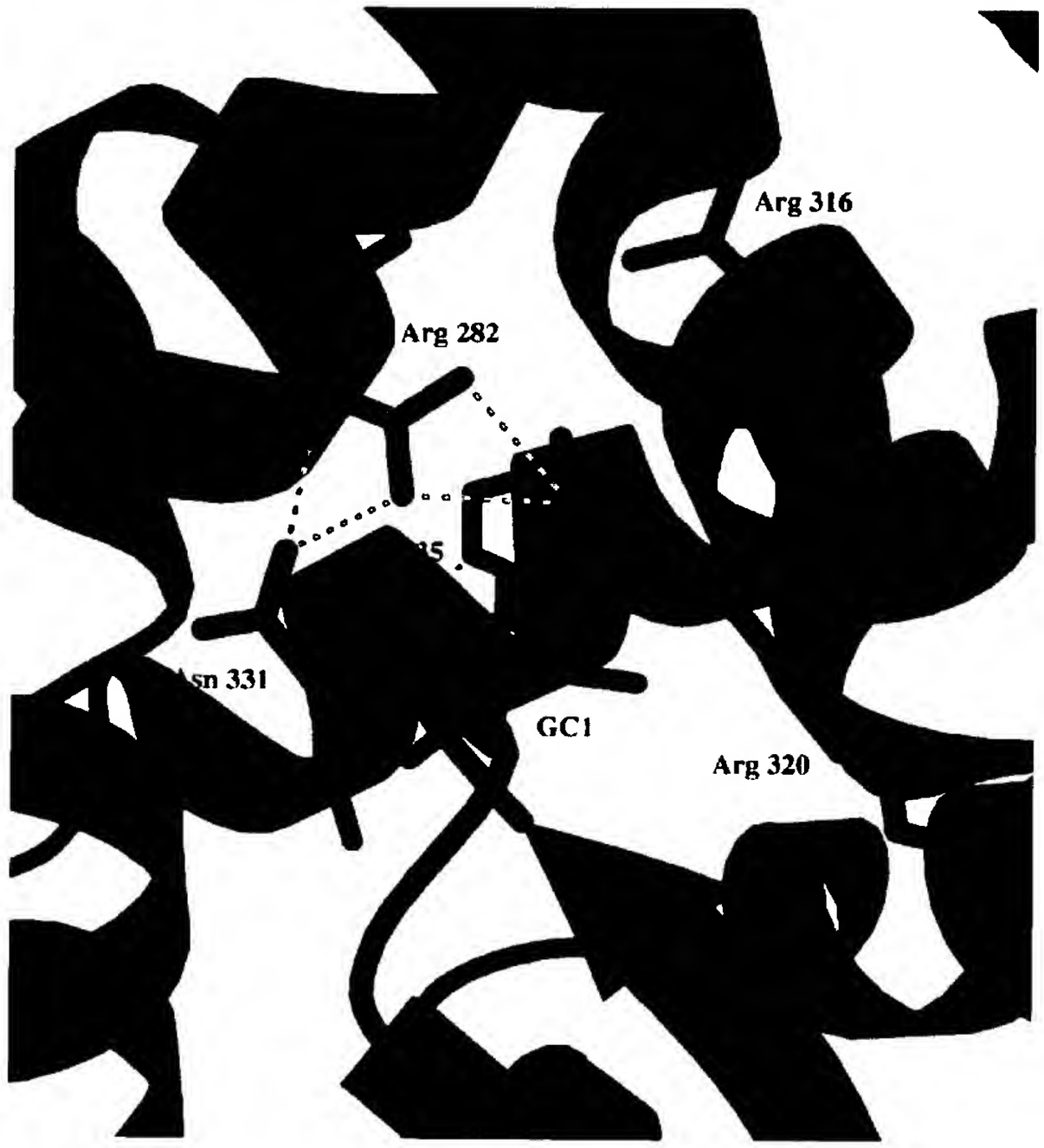


FIG. 27

Thyroid Hormone Receptor Beta with Triac

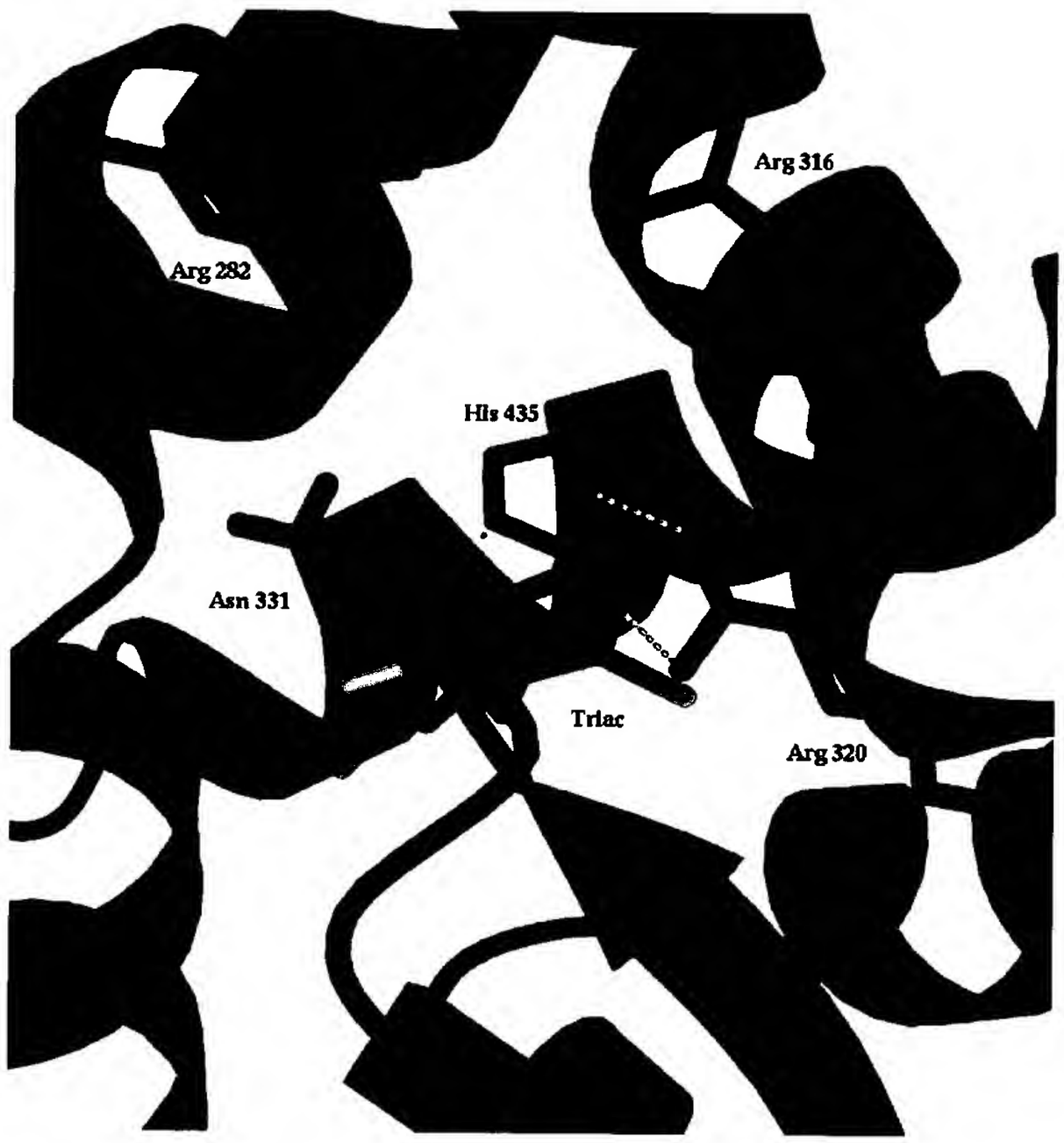


FIG. 28

BY

FTSMA

Structural Differences Between TR-b with GC1 and TR-a with Dimit

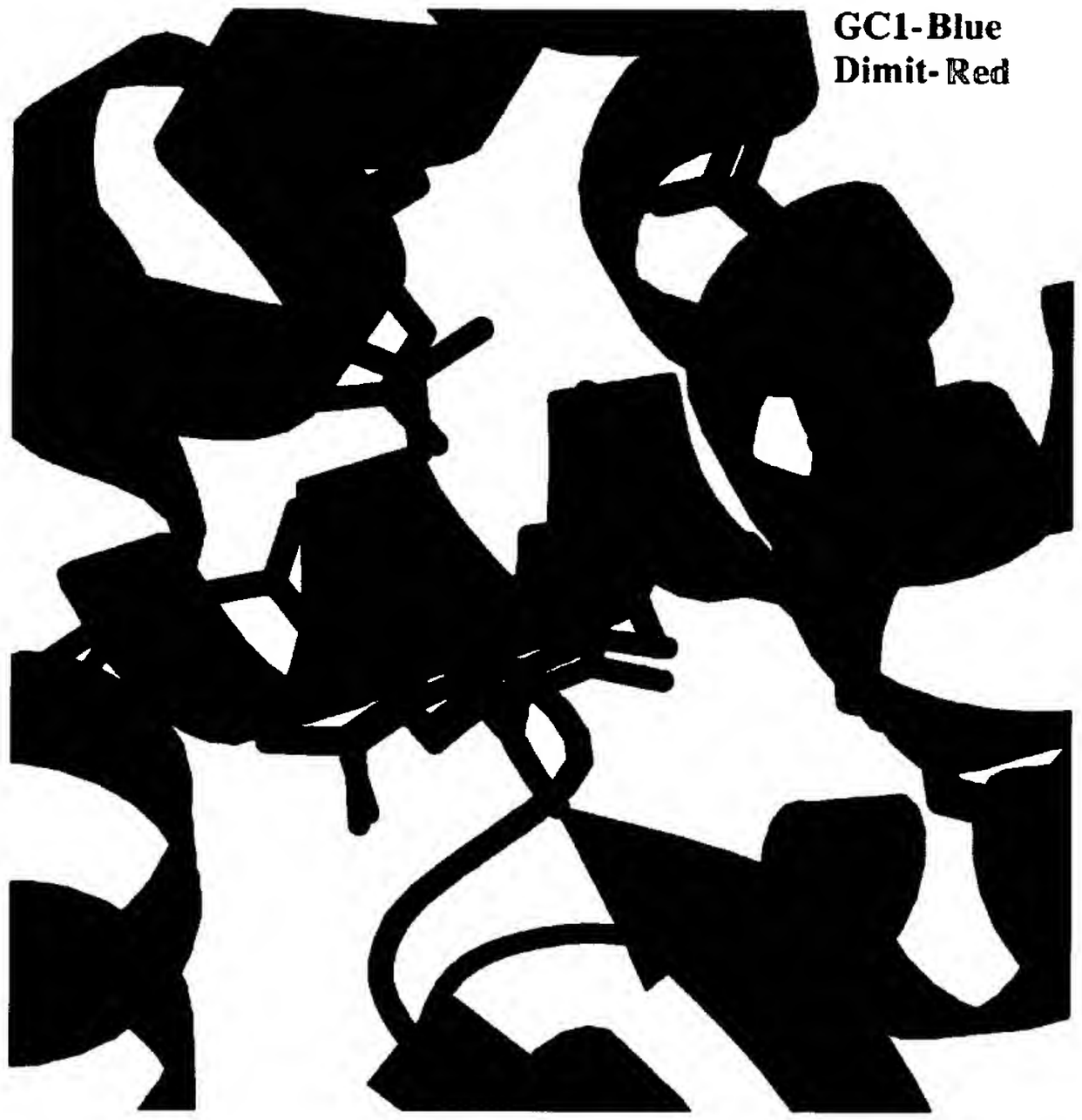


FIG. 29

Structural Differences between TR LBD isoforms with Triac

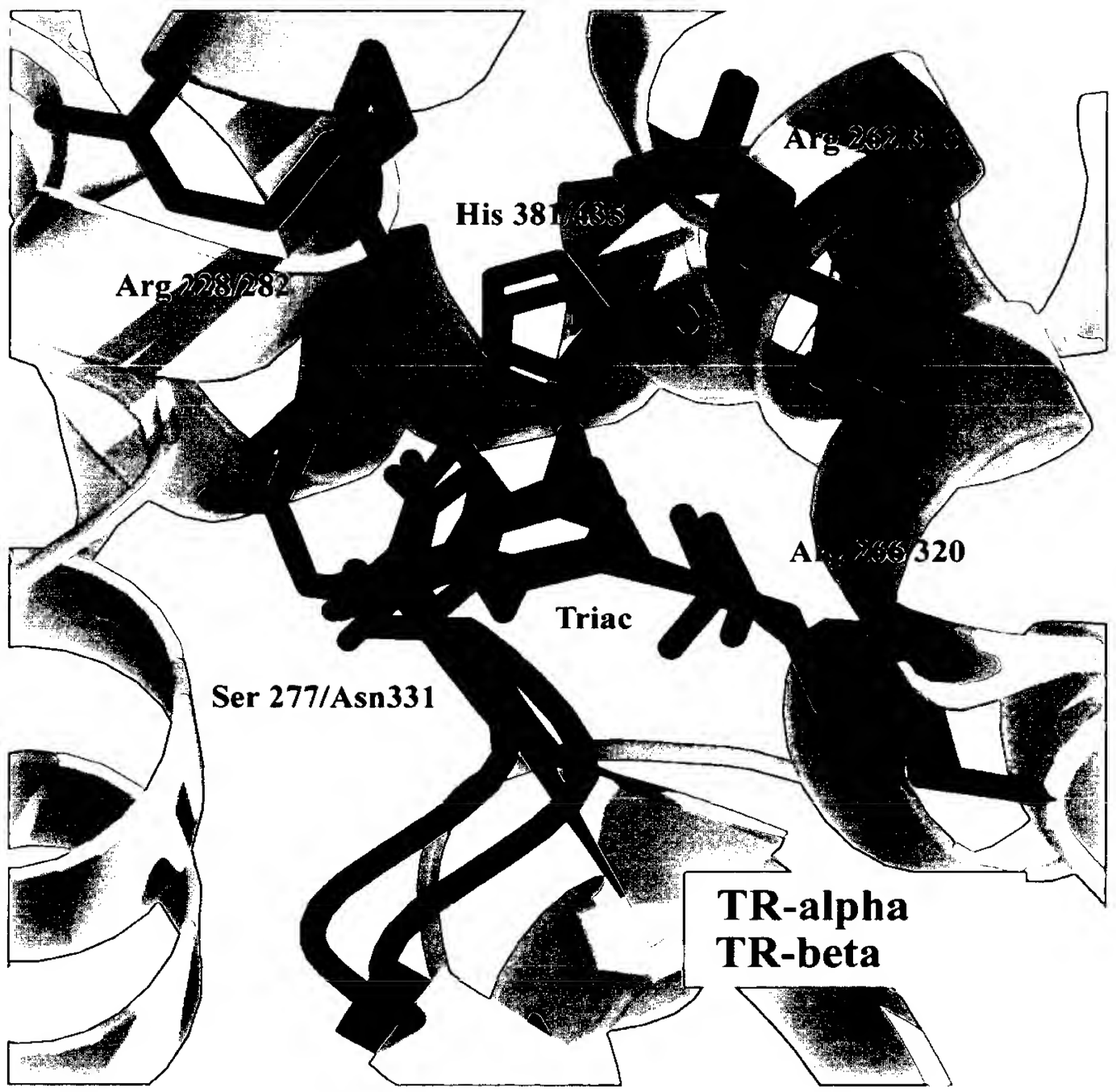
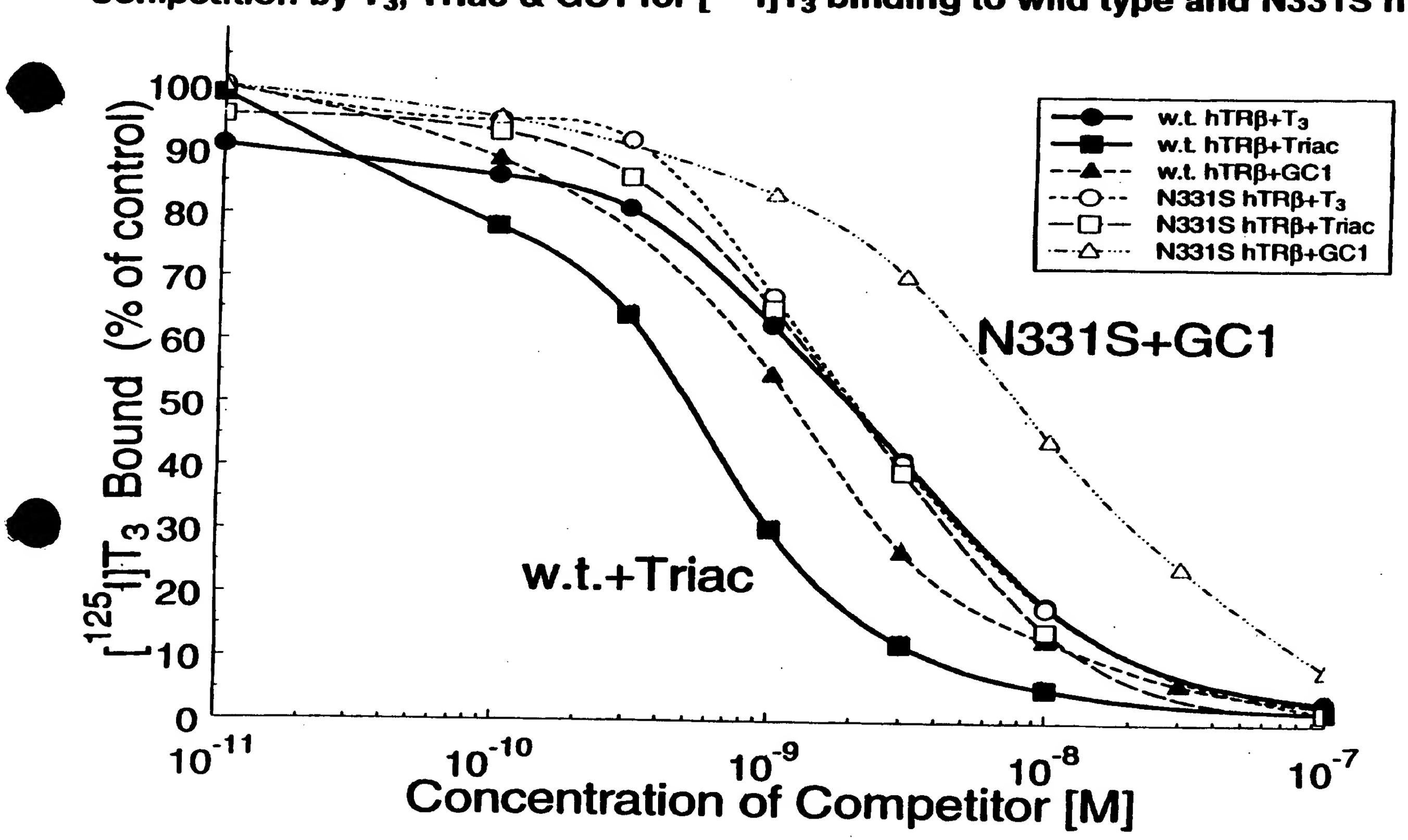


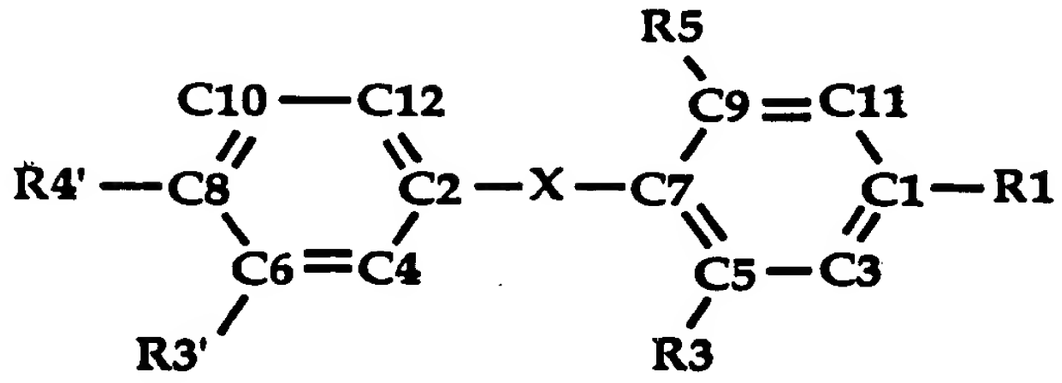
FIG. 30

FIG.31



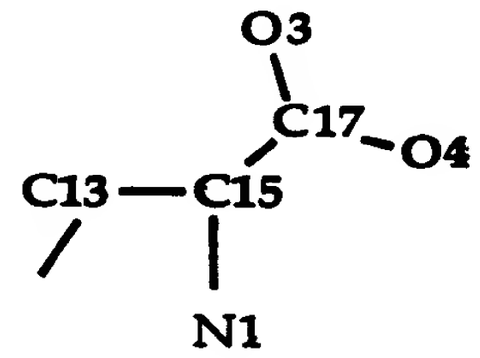
APPROVED BY DRAFTSMAN	O G. FIG.	
	CLASS	SUBCLASS

Atomic Numbering for Thyronine-like Ligands

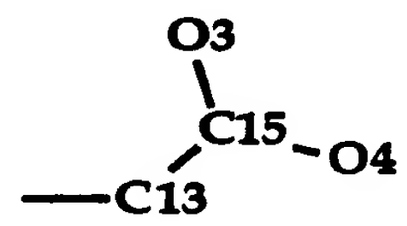


Ligand	R1	R3	R5	X	R3'	R4'
Dimit	amino propionic	C19	C20	O2	iPr	O1
$IpBr_2$	amino propionic	BR1	BR2	O2	iPr	O1
T_3	amino propionic	I1	I3	O2	I2	O1
Triac	acetic acid	I1	I3	O2	I2	O1
GC1	oxyacetic acid	C19	C20	C21	iPr	O1

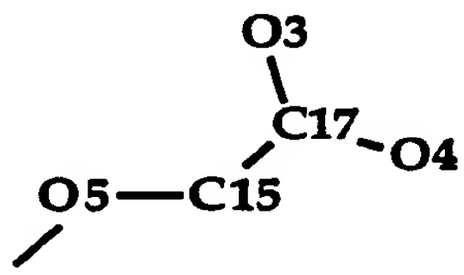
amino propionic acid



acetic acid



oxyacetic acid



isopropyl

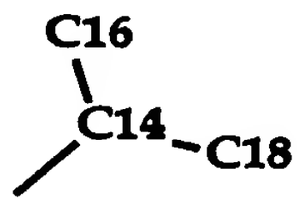


FIG.32

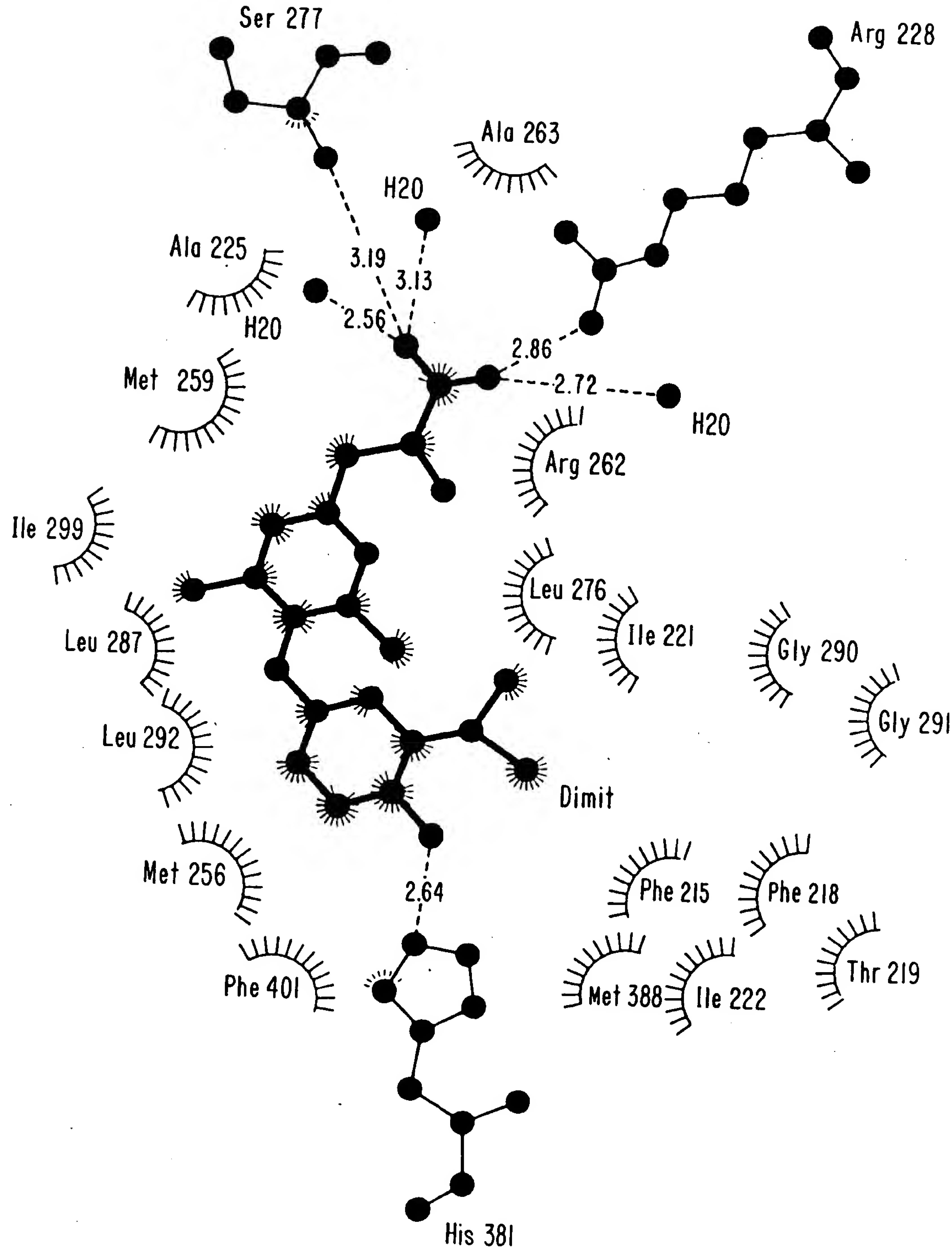

Ser 277
Arg 228
Ala 263
H20
Ala 225
3.19
3.13
2.56
H20
2.86
Met 259
2.72
H20
Arg 262
Ile 299
Leu 276
Ile 221
Gly 290
Leu 287
Gly 291
Leu 292
Dimit
Met 256
2.64
Phe 215
Phe 218
Phe 401
Met 388
Ile 222
Thr 219
His 381

FIG.6

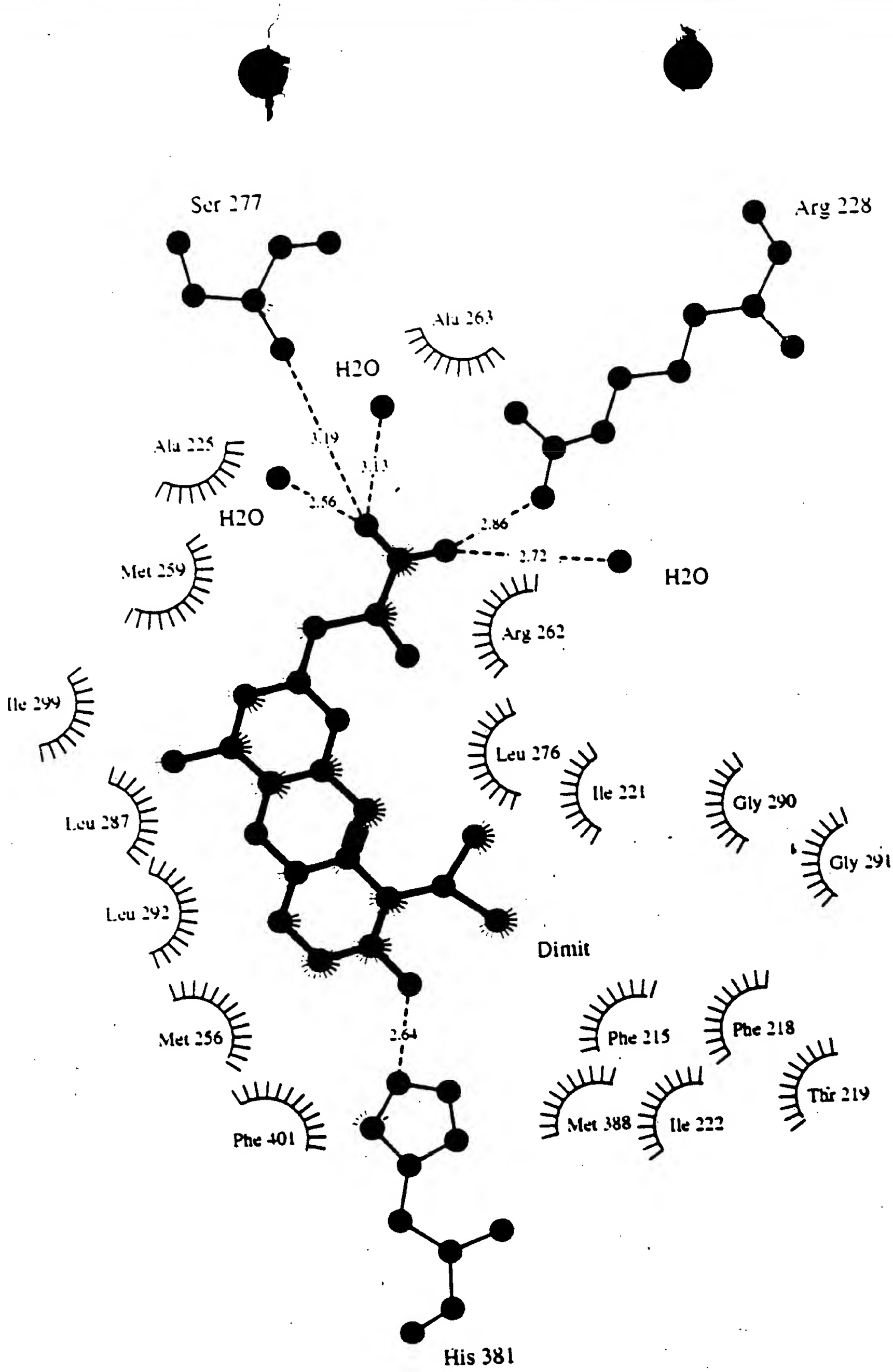

Ser 277
Arg 228
Ala 263
H2O
3.19
3.13
Ala 225
2.56
2.86
2.72
H2O
H2O
Met 259
Arg 262
Ile 299
Leu 276
Ile 221
Gly 290
Gly 291
Leu 287
Leu 292
Dimit
Met 256
2.64
Phe 215
Phe 218
Thr 219
Met 388
Ile 222
Phe 401
His 381

Figure 6